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in section 3.2 and new reference (Kjaer et al., 2004))

Glyphosate and AMPA in Drinking-water

Background document for development of
WHO Guidelines for Drinking-water Quality

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Preface

One of the primary goals of WHO and its member states is that “all people, whatever their stage of development and their social and economic conditions, have the right to have access to an adequate supply of safe drinking water.” A major WHO function to achieve such goals is the responsibility “to propose ... regulations, and to make recommendations with respect to international health matters”

The first WHO document dealing specifically with public drinking-water quality was published in 1958 as *International Standards for Drinking-water*. It was subsequently revised in 1963 and in 1971 under the same title. In 1984–1985, the first edition of the *WHO Guidelines for Drinking-water Quality* (GDWQ) was published in three volumes: Volume 1, Recommendations; Volume 2, Health criteria and other supporting information; and Volume 3, Surveillance and control of community supplies. Second editions of these volumes were published in 1993, 1996 and 1997, respectively. Addenda to Volumes 1 and 2 of the second edition were published in 1998, addressing selected chemicals. An addendum on microbiological aspects reviewing selected microorganisms was published in 2002.

The GDWQ are subject to a rolling revision process. Through this process, microbial, chemical and radiological aspects of drinking-water are subject to periodic review, and documentation related to aspects of protection and control of public drinking-water quality is accordingly prepared/updated.

Since the first edition of the GDWQ, WHO has published information on health criteria and other supporting information to the GDWQ, describing the approaches used in deriving guideline values and presenting critical reviews and evaluations of the effects on human health of the substances or contaminants examined in drinking-water.

For each chemical contaminant or substance considered, a lead institution prepared a health criteria document evaluating the risks for human health from exposure to the particular chemical in drinking-water. Institutions from Canada, Denmark, Finland, France, Germany, Italy, Japan, Netherlands, Norway, Poland, Sweden, United Kingdom and United States of America prepared the requested health criteria documents.

Under the responsibility of the coordinators for a group of chemicals considered in the guidelines, the draft health criteria documents were submitted to a number of scientific institutions and selected experts for peer review. Comments were taken into consideration by the coordinators and authors before the documents were submitted for final evaluation by the experts meetings. A “final task force” meeting reviewed the health risk assessments and public and peer review comments and, where appropriate, decided upon guideline values. During preparation of the third edition of the GDWQ, it was decided to include a public review via the world wide web in the process of development of the health criteria documents.

During the preparation of health criteria documents and at experts meetings, careful consideration was given to information available in previous risk assessments carried out by the International Programme on Chemical Safety, in its Environmental Health Criteria monographs and Concise International Chemical Assessment Documents, the International Agency for Research on Cancer, the joint FAO/WHO Meetings on Pesticide Residues and the joint FAO/WHO Expert Committee on Food Additives (which evaluates contaminants such as lead, cadmium, nitrate and nitrite in addition to food additives).

Further up-to-date information on the GDWQ and the process of their development is available on the WHO internet site and in the current edition of the GDWQ.

Acknowledgements

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The work of the following working group coordinators was crucial in the development of this document and others in the third edition:

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The contribution of peer reviewers is greatly appreciated. The draft text was posted on the world wide web for comments from the public. The revised text and the comments were discussed at the Final Task Force Meeting for the third edition of the GDWQ, held on 31 March to 4 April 2003, at which time the present version was finalized. The input of those who provided comments and of participants in the meeting is gratefully reflected in the final text.

The WHO coordinators were as follows:

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Ms Marla Sheffer of Ottawa, Canada, was responsible for the scientific editing of the document.

Many individuals from various countries contributed to the development of the GDWQ. The efforts of all who contributed to the preparation of this document and in particular those who provided peer or public domain review comment are greatly appreciated.

Acronyms and abbreviations used in the text

ADI	acceptable daily intake
AMPA	aminomethylphosphonic acid
CAS	Chemical Abstracts Service
FAO	Food and Agriculture Organization of the United Nations
IPCS	International Programme on Chemical Safety
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
LD ₅₀	median lethal dose
NOAEL	no-observed-adverse-effect level
USA	United States of America
WHO	World Health Organization

Table of contents

1. GENERAL DESCRIPTION	1
1.1 Identity	1
1.2 Physicochemical properties of glyphosate.....	1
1.3 Major uses.....	1
1.4 Environmental fate.....	1
2. ANALYTICAL METHODS	2
3. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE.....	2
3.1 Air	2
3.2 Water.....	3
3.3 Food	3
3.4 Estimated total exposure and relative contribution of drinking-water.....	3
4. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS	4
5. EFFECTS ON EXPERIMENTAL ANIMALS AND <i>IN VITRO</i> TEST SYSTEMS.....	4
5.1 Acute exposure.....	4
5.2 Short-term exposure.....	4
5.3 Long-term exposure and carcinogenicity.....	5
5.4 Reproductive and developmental toxicity	6
5.5 Mutagenicity and related end-points.....	7
5.6 Toxicity of AMPA	7
6. EFFECTS ON HUMANS.....	9
7. CONCLUSIONS.....	9
8. REFERENCES	9

1. GENERAL DESCRIPTION

1.1 Identity

	<i>Glyphosate</i>	<i>AMPA</i>
CAS No.:	1071-83-6	1066-51-9
Molecular formula:	C ₃ H ₈ NO ₅ P	CH ₆ NO ₃ P

The IUPAC name for glyphosate is *N*-(phosphonomethyl)glycine. Glyphosate is a weak organic acid; it consists of a glycine moiety and a phosphonomethyl moiety.

The primary degradation product of glyphosate in plants, soil and water is aminomethylphosphonic acid (AMPA), whose chemical structure is very similar to that of glyphosate (see below).



1.2 Physicochemical properties of glyphosate (IPCS, 1994)

<i>Property</i>	<i>Value</i>
Vapour pressure	<10 ⁻⁵ Pa at 25 °C (negligible)
Melting point	185 °C (decomposes at 199 °C)
Log <i>n</i> -octanol/water partition coefficient	-2.8
Water solubility	10.1 g/litre at 20 °C
Specific gravity	1.70 g/cm ³

1.3 Major uses

Glyphosate is a broad-spectrum post-emergence herbicide. It has a high activity when applied to foliage, and it is used worldwide in both agriculture and forestry. Glyphosate is also used for aquatic weed control (IPCS, 1994). AMPA has no commercial use.

1.4 Environmental fate

Glyphosate is strongly bound to soil particles and is not taken up by the roots of plants. It is metabolized very little by plants, the major metabolite being AMPA. Glyphosate readily translocates from treated foliage to other parts of the plant. Residues from treated weeds passing into the soil are not taken up by other plants (FAO/WHO, 1986).

Microbial biodegradation of glyphosate occurs in soil, aquatic sediment and water. The main route of biodegradation of glyphosate appears to be by splitting the C–N bond to produce AMPA, the principal microbial metabolite; AMPA is also

GLYPHOSATE AND AMPA IN DRINKING-WATER

biologically degradable, with liberation of carbon dioxide. Degradation occurs more rapidly in aerobic than in anaerobic conditions. Half-lives for biodegradation in soil vary widely and range between a few days and several months; in water, half-lives between 12 h and 7 weeks have been measured (CCME, 1989).

Glyphosate is chemically stable in water and is not subject to photochemical degradation (FAO/WHO, 1986). The low mobility of glyphosate in soil indicates a minimal potential for the contamination of groundwater. Glyphosate can, however, enter surface and subsurface waters by direct use near aquatic environments or by runoff or leaching from terrestrial applications. This has been substantiated by reports that indicate the presence of glyphosate residues in water from direct overspray in forestry operations, from runoff and from irrigation canal discharges. Furthermore, the possibility of aquatic contamination from drift during agricultural or silvicultural applications also exists. Depending upon the suspended solids loading and the microbial activity of flowing water, glyphosate may be transported several kilometres downstream from the site of aquatic application (CCME, 1989).

Glyphosate is not expected to bioaccumulate in food in view of its high water solubility and its ionic character. Although residues of glyphosate were found in fish, crustaceans and molluscs after exposure to water containing glyphosate, residues declined to about 50–90% of the accumulated levels when these aquatic organisms were subsequently exposed to water free from glyphosate for 14–28 days (FAO/WHO, 1986).

2. ANALYTICAL METHODS

Various analytical methods for the determination of glyphosate have been described, including thin-layer chromatography, high-performance liquid chromatography and gas chromatography–mass spectrometry. The limits of determination were 0.02–50 µg/litre in water, 0.05–1 mg/kg in soil, 0.01–0.05 mg/kg in plants and about 0.3 µg/m³ in air. The limit of determination of AMPA in water is reported to be 1.2 µg/litre (IPCS, 1994).

3. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

3.1 Air

Concentrations in air are available only from studies on exposures of workers involved in application of the herbicide. Air concentrations during silvicultural spraying were mostly below 1.3 µg/m³; the highest value observed was 15.7 µg/m³. The highest estimated exposure (dermal and inhalation) of about 8000 µg/h, as reported in a study with spray applicators, corrected for incomplete absorption, equals about 40 µg/kg of body weight per day (8-h working day for a 60-kg adult) (IPCS, 1994).

3.2 Water

In a survey conducted in 1988–1989 in the Netherlands, surface water contained 0.5–1 µg of glyphosate per litre and 6 µg of the metabolite AMPA per litre (IPCS, 1994). In Canada, glyphosate residues as high as 5153 µg/litre were measured after direct aerial application over lakes, ponds or streams. Glyphosate concentrations in water declined to a few µg/litre or to non-detectable levels hours or days post-treatment, depending on the extent of vegetation present. The concentration of AMPA in water without substantial vegetation was about 3 µg/litre (CCME, 1989). In the USA, pond water contained 90–1700 µg of glyphosate per litre and 2–35 µg of AMPA per litre, whereas stream water contained 35–1237 and <1.0–10 µg of glyphosate and AMPA, respectively, per litre (IPCS, 1994). Intensive monitoring studies over a number of years in Denmark have identified glyphosate and AMPA in the root zone and in groundwater at monitoring sites; however, the concentrations in groundwater were less than 0.1 µg/litre (Kjaer et al., 2004).

3.3 Food

No information was available on direct measurements of glyphosate in foodstuffs (as part of food surveillance) or total diets. The only information available comes from residue levels resulting from supervised trials. In pre-planting use of glyphosate, residues of glyphosate and its metabolite were not detected (<0.05 mg/kg) in cereal grains at harvest. Pre-harvest application of glyphosate to cereals and pulses resulted in mean residue levels ranging from 0.2 to 4.8 mg/kg, when the glyphosate was used according to good agricultural practice. Industrial processing of wheat to flour resulted in a decrease in glyphosate level from 1.6 to 0.16 mg/kg (FAO/WHO, 1986).

Fish exposed to water containing 10 mg of glyphosate per litre for 14 days contained 0.2–0.7 mg of glyphosate per kg. Residues were reduced when fish were exposed to glyphosate-free water. In controlled feeding studies, mean residues of glyphosate found in muscle tissues of pigs, poultry and cattle were <0.05 mg/kg. Livers of these animals contained up to 0.12 mg/kg, whereas residues in cattle milk were not detectable (FAO/WHO, 1986).

3.4 Estimated total exposure and relative contribution of drinking-water

Use of glyphosate as a herbicide may result in the presence of residues in air, drinking-water, crops and animal tissues destined for human consumption. Main routes of exposure to glyphosate are expected to be inhalation and dermal exposure in the occupational setting and consumption of water and food for the general population. Because of its sorption to particulate matter and its microbial degradation in the aquatic environment (CCME, 1989), the major source of exposure to glyphosate is expected to be food.

GLYPHOSATE AND AMPA IN DRINKING-WATER

4. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

The results of oral studies with [¹⁴C]glyphosate in rats, rabbits and goats indicate that absorption from the gastrointestinal tract is incomplete and amounts to approximately 30% of the dose or less.

On day 7 after administration of a single oral dose of [¹⁴C]glyphosate to rats, the isotope was widely distributed throughout the body, with the highest concentration found in the bones.

Biotransformation of glyphosate occurs to a very low degree only. In rats, it was shown that almost all of the ¹⁴C in urine and faeces, after a single oral administration of [¹⁴C]glyphosate, was present as unchanged parent compound. Elimination through exhaled air is very low. AMPA was the only metabolite, accounting for only 0.2–0.3% of the applied dose of [¹⁴C]glyphosate (IPCS, 1994).

In a study of the metabolic fate of AMPA in rats, AMPA was only moderately absorbed (approximately 20%); excretion was almost exclusively via the urine, with less than 0.1% of the dose expired as carbon dioxide (FAO/WHO, 1987).

5. EFFECTS ON EXPERIMENTAL ANIMALS AND IN VITRO TEST SYSTEMS

5.1 Acute exposure

Glyphosate and its formulations have very low acute toxicity by the oral and dermal administration routes. Median oral lethal doses (LD₅₀s) of glyphosate range from 1950 to >5000 mg/kg of body weight for mice, rats and goats (IPCS, 1994). Glyphosate has been classified by WHO (1996) as unlikely to present an acute hazard in normal use.

5.2 Short-term exposure

In a 13-week feeding study, groups of 15 male and 15 female Charles River CD-1 mice were fed technical glyphosate (purity 98.7%) in their diet at dose levels of 0, 0.5, 1.0 or 5.0%. No effect on appearance or survival was observed. Growth retardation and increased weights of brain, heart and kidneys were observed at 5.0%. Liver weights were increased at 1.0% and 5.0%. Limited histopathology showed no adverse effects. The authors of the study concluded that the NOAEL was 1.0% glyphosate in the diet, equal to 1890 mg/kg of body weight per day (Bio/Dynamics Inc., 1979; FAO/WHO, 1987; IPCS, 1994).

In a 13-week feeding study, Sprague-Dawley rats received 0.1, 0.5 or 2% technical glyphosate in their diet. No effects on appearance, survival or growth were observed. Haematology, blood biochemistry and urinalysis, carried out at test end only, were also unaffected. Organ weights determined for liver, kidneys and testes were not affected. Limited histopathology showed no adverse effect in any tissue. The NOAEL

GLYPHOSATE AND AMPA IN DRINKING-WATER

in this study was 2% glyphosate in the diet (the highest dose tested), equal to 1267 mg/kg of body weight per day (Monsanto, 1987).

Two further 13-week studies in rodents were conducted. Both mice (B6C3F₁) and rats (F-344/N) were administered glyphosate (purity approximately 99%) in feed at levels of 0, 3125, 6250, 12 500, 25 000 or 50 000 mg/kg (NTP, 1992). In mice, reduced weight gains were observed at 50 000 mg/kg of diet in both sexes. Dose-dependent lesions in the parotid gland were observed at 6250 mg/kg of feed and higher but were not seen at the lowest dose level tested. The NOAEL in this study was 3125 mg/kg of feed, equal to 507 mg/kg of body weight per day (NTP, 1992).

In rats, reduced weight gains were observed in males at 25 000 mg/kg of feed and in both sexes at 50 000 mg/kg of feed. Clinical chemistry showed increased alkaline phosphatase and alanine aminotransferase at 6250 mg/kg of feed in males and at 12 500 mg/kg of feed in females. Decreases in sperm count were observed in males at 25 000 and 50 000 mg/kg of feed. Cytoplasmic alterations of the parotid and submandibular salivary glands, consisting of basophilic changes and hypertrophy of acinar cells, were observed. Effects on the salivary glands were observed at the lowest dose tested (3125 mg/kg of feed, equal to 205 mg/kg of body weight per day for males and 213 mg/kg of body weight per day for females). Thus, a NOAEL could not be identified in this study (NTP, 1992).

Groups of six male and six female beagle dogs were administered technical glyphosate (96.1% pure) in gelatin capsules at dose levels of 0, 20, 100 or 500 mg/kg of body weight per day for 52 weeks. No effects were observed with respect to clinical signs, body weight, feed consumption, ophthalmoscopy, haematology, urinalysis, gross pathology and histopathology. The NOAEL in this study was 500 mg/kg of body weight per day, the highest dose tested (FAO/WHO, 1987; IPCS, 1994).

5.3 Long-term exposure and carcinogenicity

In a combined chronic toxicity and carcinogenicity study, groups of Charles River CD-1 mice (50 per sex per group) were fed technical glyphosate in the diet for 24 months at levels of 0, 0.1, 0.5 or 3.0%. No effect on survival or appearance was noted. Body weights were decreased in the males of the high-dose group. Haematology and organ weights showed no effects. Histopathology in liver revealed an increased incidence of central lobular hepatocyte hypertrophy and hepatocyte necrosis among high-dose males. Hyperplasia of the urinary bladder was increased in frequency in mid- and high-dose males (incidences: 3/49, 3/50, 10/50, and 8/50), but not in treated females. There were no statistically significant increases in the frequency of neoplastic lesions. The NOAEL in this study was 0.5% glyphosate, equal to 814 mg/kg of body weight per day (Bio/Dynamics Inc., 1983).

Groups of Charles River Sprague-Dawley rats (50 per sex per dose) were fed technical glyphosate in their diets at dose levels of about 0, 3, 10 or 32 mg/kg of body weight per day for 26 months. Survival, appearance, haematology, blood

GLYPHOSATE AND AMPA IN DRINKING-WATER

biochemistry, urinalysis and organ weights were not changed. Slight growth retardation during part of the study was noted in the high-dose males. The incidence of interstitial cell tumours in testes showed a statistically significant increase (incidences: 0/50, 3/50, 1/50 and 6/50; historical control range: 3–7%) (Bio/Dynamics Inc., 1981a). This finding, in itself constituting evidence of a carcinogenic effect in rats, should be judged in light of the absence of an effect at much higher dose levels in the more recent 2-year study in rats (see below). This is also valid for the slight growth retardation. The NOAEL was 32 mg/kg of body weight per day, the highest dose tested (Bio/Dynamics Inc., 1981a).

In the recent 2-year study, groups of Charles River Sprague-Dawley rats (60 per sex per dose) were fed technical glyphosate in their diets at dose levels of about 0, 100, 410 or 1060 mg/kg of body weight per day for 24 months. There was no effect on survival or appearance. Growth was retarded in the high-dose females. Haematology and blood biochemistry showed no effects. In the high-dose males, the urine specific gravity and urine pH were increased. A statistically significant increased incidence of degenerative lens changes was found among the high-dose males; however, this finding was within the historical control range. Liver weights were increased in the high-dose males only. Increased incidence of inflammation of the gastric squamous mucosa was observed in the mid- and high-dose groups (incidences in males: 2/58, 3/58, 5/59 and 7/59; females: 0/59, 3/60, 9/60 and 6/59; historical range: 0–13.3%). The incidence of pancreatic islet cell adenomas was increased (statistically significant) among low- and high-dose animals. However, these effects were within the historical control range. No pancreatic carcinomas were found. The NOAEL in this study was 410 mg/kg of body weight per day (Monsanto, 1990a).

5.4 Reproductive and developmental toxicity

Groups of female Charles River CD-1 rats were administered technical glyphosate by gavage at dose levels of 0, 300, 1000 or 3500 mg/kg of body weight per day on days 6–19 of gestation. At 3500 mg/kg of body weight per day, the following effects were observed: increased incidence of soft stools, diarrhoea, breathing rattles, red nasal discharge, reduced activity, increased mortality (6/25 dams dying before the end of the treatment period), growth retardation, increased incidence of early resorptions, decreases in total number of implantations and the number of viable fetuses, and increased number of fetuses with reduced ossification of sternbrae. At the lower dose levels, these effects were absent. The NOAEL in this study was 1000 mg/kg of body weight per day (IRDC, 1980a).

Groups of 16 female Dutch belted rabbits received technical glyphosate by gavage in 0.5% Methocel at dose levels of 0, 75, 175 or 350 mg/kg of body weight per day on days 6–27 of gestation. The control group received the vehicle only. The incidence of diarrhoea and soft stools was increased in the high-dose group and also, to a slight degree, in the mid-dose group. The incidence of nasal discharge was increased in the high-dose group only. In the mid- and high-dose groups, 2 and 10 dams, respectively, died during the study from unknown causes. The IPCS Task Group concluded that the NOAEL was 175 mg/kg of body weight per day (IRDC, 1980a; IPCS, 1994).

In a three-generation study, groups of Sprague-Dawley rats were given glyphosate (98.7% pure) in the diet at doses of 0, 3, 10 or 30 mg/kg of body weight per day for 60 days. The only effect noted was an increased incidence of unilateral renal tubular dilation in the F_{3b} male pups of the high-dose group (incidence not determined in mid-dose group; earlier litters not examined). The NOAEL in this study was 30 mg/kg of body weight per day, the highest dose tested (Bio/Dynamics Inc., 1981b; IPCS, 1994).

In a more recent two-generation feeding study, Sprague-Dawley rats received glyphosate at doses of 0, 100, 500 or 1500 mg/kg of body weight per day. Soft stools and decreased body weights in parent animals and slightly decreased litter size and pup weights were seen in the high-dose group. Decreased body weights of parents and pups were seen to a slight degree in the mid-dose group. No histological effect on kidneys was present in the F_{2b} male pups (15 and 23 pups examined in control and high-dose groups, respectively; first generation and F_{2a} pups not examined). The NOAEL in this study was 500 mg/kg of body weight per day (Monsanto, 1990b; IPCS, 1994).

In its evaluation of these latter two reproductive toxicity studies, the IPCS Task Group noted that the number of pups submitted to histopathological examination in both studies was limited. These limitations made it difficult to evaluate the renal effect seen in pups at 30 mg/kg of body weight per day in the Bio/Dynamics Inc. (1981b) study (IPCS, 1994).

5.5 Mutagenicity and related end-points

Glyphosate was consistently without mutagenic effect in a range of genotoxicity assays *in vitro* and *in vivo* (IPCS, 1994).

5.6 Toxicity of AMPA¹

AMPA is slightly hazardous to rats given a single oral dose, with an LD₅₀ of 8300 mg/kg of body weight (WHO, 1996).

In a 90-day study of toxicity, rats received AMPA in the diet at 0, 400, 1200 or 4800 mg/kg of body weight per day. A significant, dose-related decrease in body weight gain was seen in males at the two highest doses and in females at the highest dose. The two highest doses also resulted in significantly increased lactate dehydrogenase activity, whereas aspartate aminotransferase activity and cholesterol levels were significantly increased only at the highest dose. Urinalysis showed a significant decrease in urinary pH and increased amounts of calcium oxalate crystals in the urine of animals at the highest dose.

Dose-related irritation of the mucosal and submucosal layers of the urinary tract, corresponding to hyperplasia of the urinary bladder, was seen in rats at 1200 and 4800

¹ This section was taken from FAO/WHO (1998).

GLYPHOSATE AND AMPA IN DRINKING-WATER

mg/kg of body weight per day, the effect being more marked in males than in females. In addition, epithelial hyperplasia in the renal pelvis was observed at the highest dose. The NOAEL was 400 mg/kg of body weight per day.

In a 90-day study of toxicity in dogs receiving AMPA at 0, 10, 30, 100 or 300 mg/kg of body weight per day in gelatin capsules, no statistically significant treatment-related changes were observed. The NOAEL was thus the highest dose, 300 mg/kg of body weight per day. It should be noted that in a 1-month range-finding study with groups of only two male and two female dogs, changes in some haematological parameters (e.g., decreased haemoglobin, packed cell volume and erythrocyte counts) were seen in animals at 300 or 1000 mg/kg of body weight per day. These effects were not reproduced in the 90-day study.

No indication of genotoxic activity was seen in studies of gene mutation in bacteria, of DNA repair in bacteria and mammalian cells *in vitro* or of micronucleus formation *in vivo*. No assays for gene mutation were performed in mammalian cells *in vitro*, but the structural similarity of AMPA to glyphosate and the lack of genotoxicity of glyphosate, including in an assay for gene mutation in mammalian cells *in vitro*, indicate that such an assay with AMPA would be redundant.

In a study of developmental toxicity, rats received AMPA at 0, 150, 400 or 1000 mg/kg of body weight per day in corn oil by gavage. Dose-related increases in the incidences of soft stools, mucoid faeces and hair loss were seen in dams at the two higher doses. Dams at the highest dose also had short periods of decreased body weight gain and food consumption. Fetal body weight was decreased at 1000 mg/kg of body weight per day. No teratogenic effects were observed. Dams at 150 mg/kg of body weight per day also had an increased incidence of soft stools; however, in the absence of any associated effects, such as hair loss or mucoid faeces, the Meeting considered this dose to be the NOAEL for maternal toxicity. The NOAEL for developmental toxicity was 400 mg/kg of body weight per day.

AMPA did not induce dermal or ocular irritation in rabbits.

No long-term study of the toxicity or carcinogenicity of AMPA has been carried out, but in the more recent of two such studies with technical-grade glyphosate in rats at dietary levels of 0.2, 0.8 or 2%, the AMPA content of the test compound was given, namely 0.68%. At the highest dose of 2% glyphosate in the diet, females showed decreased body weight gain and males showed an increased incidence of degenerative lenticular changes. The NOAEL for technical-grade glyphosate was 0.8% in the diet, corresponding to 400 mg/kg of body weight per day for glyphosate and 2.7 mg/kg of body weight per day for AMPA. No increase in tumour incidence was seen in this study.

No multigeneration study of the reproductive toxicity of AMPA has been reported, but in a recent two-generation study in rats with technical-grade glyphosate at dietary levels of 0.2, 1 or 3%, the test compound contained 0.61% AMPA. At the highest dose, soft stools, decreased parental body weights, slightly decreased litter sizes and

GLYPHOSATE AND AMPA IN DRINKING-WATER

decreased pup weights were observed. The NOAEL was 1% in the diet, corresponding to 740 mg of glyphosate per kg of body weight per day and 4.5 mg of AMPA per kg of body weight per day.

6. EFFECTS ON HUMANS

Several cases of (mostly intentional) intoxications with technical glyphosate herbicide formulation have been reported. A typical symptom is erosion of the gastrointestinal tract. No compound-related effects were observed in a test group of five applicators prior to and after exposure for 1 week. No controlled studies have been conducted in humans.

7. CONCLUSIONS

Glyphosate and AMPA have very similar chemical structures. Studies of the metabolism of glyphosate in experimental animals indicate that essentially none is biotransformed into AMPA. The 1997 JMPR Meeting (FAO/WHO, 1998) compared the toxicity profile of AMPA with that of glyphosate and concluded that the major targets of the toxicity of AMPA had been investigated. The results showed little toxicity. JMPR concluded that the two compounds have similar toxicological profiles and considered that a full database on AMPA is unnecessary. AMPA was considered to be of no greater toxicological concern than its parent compound.

JMPR established a group ADI for AMPA alone or in combination with glyphosate of 0.3 mg/kg of body weight, based upon a NOAEL of 32 mg/kg of body weight per day, the highest dose tested, identified in a 26-month study of toxicity in rats fed technical-grade glyphosate and using an uncertainty factor of 100. A health-based value of 0.9 mg/litre can be derived based on the ADI of 0.3 mg/kg of body weight, assuming a 60-kg adult consuming 2 litres of drinking-water per day, and allocating 10% of the ADI to drinking-water.

Because of their low toxicity, the health-based value derived for AMPA alone or in combination with glyphosate is orders of magnitude higher than concentrations of glyphosate or AMPA normally found in drinking-water. Under usual conditions, therefore, the presence of glyphosate and AMPA in drinking-water does not represent a hazard to human health. For this reason, the establishment of a numerical guideline value for glyphosate and AMPA is not deemed necessary.

8. REFERENCES

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GLYPHOSATE AND AMPA IN DRINKING-WATER

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