Annotate abstracts and methods sections.

Classify study as: ANIMAL, HUMAN, INVITRO, OTHER.

An ANIMAL abstract:

[Reproduction.](https://www.ncbi.nlm.nih.gov/pubmed/27486271" \o "Reproduction (Cambridge, England).) 2016 Nov;152(5):403-15. doi: 10.1530/REP-16-0171. Epub 2016 Aug 2.

# Effects of neonatal exposure to a glyphosate-based herbicide on female rat reproduction.

[Ingaramo PI](https://www.ncbi.nlm.nih.gov/pubmed/?term=Ingaramo%20PI%5BAuthor%5D&cauthor=true&cauthor_uid=27486271)1, [Varayoud J](https://www.ncbi.nlm.nih.gov/pubmed/?term=Varayoud%20J%5BAuthor%5D&cauthor=true&cauthor_uid=27486271)1, [Milesi MM](https://www.ncbi.nlm.nih.gov/pubmed/?term=Milesi%20MM%5BAuthor%5D&cauthor=true&cauthor_uid=27486271)1, [Schimpf MG](https://www.ncbi.nlm.nih.gov/pubmed/?term=Schimpf%20MG%5BAuthor%5D&cauthor=true&cauthor_uid=27486271)1, [Muñoz-de-Toro M](https://www.ncbi.nlm.nih.gov/pubmed/?term=Mu%C3%B1oz-de-Toro%20M%5BAuthor%5D&cauthor=true&cauthor_uid=27486271)1, [Luque EH](https://www.ncbi.nlm.nih.gov/pubmed/?term=Luque%20EH%5BAuthor%5D&cauthor=true&cauthor_uid=27486271)2.

### Abstract

In this study, we investigated whether neonatal exposure to a glyphosate-based herbicide (GBH) alters the reproductive performance and the molecular mechanisms involved in the decidualization process in adult rats. Newborn female rats received vehicle or 2 mg/kg/day of a GBH on postnatal days (PND) 1, 3, 5 and 7. On PND90, the rats were mated to evaluate (i) the reproductive performance on gestational day (GD) 19 and (ii) the ovarian steroid levels, uterine morphology, endometrial cell proliferation, apoptosis and cell cycle regulators, and endocrine pathways that regulate uterine decidualization (steroid receptors/COUP-TFII/Bmp2/Hoxa10) at the implantation sites (IS) on GD9. The GBH-exposed group showed a significant increase in the number of resorption sites on GD19, associated with an altered decidualization response. In fact, on GD9, the GBH-treated rats showed morphological changes at the IS, associated with a decreased expression of estrogen and progesterone receptors, a downregulation of COUP-TFII (Nr2f2) and Bmp2 mRNA and an increased expression of HOXA10 and the proliferation marker Ki67(Mki67) at the IS. We concluded that alterations in endometrial decidualization might be the mechanism of GBH-induced post-implantation embryo loss.

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PMID: [27486271](https://www.ncbi.nlm.nih.gov/pubmed/27486271) DOI: [10.1530/REP-16-0171](https://dx.doi.org/10.1530/REP-16-0171)

A HUMAN abstract:

[Environ Health Perspect.](https://www.ncbi.nlm.nih.gov/pubmed/27285288" \o "Environmental health perspectives.) 2016 Jun 10. [Epub ahead of print]

# Rheumatoid Arthritis in Agricultural Health Study Spouses: Associations with Pesticides and Other Farm Exposures.

[Parks CG](https://www.ncbi.nlm.nih.gov/pubmed/?term=Parks%20CG%5BAuthor%5D&cauthor=true&cauthor_uid=27285288)1, [Hoppin JA](https://www.ncbi.nlm.nih.gov/pubmed/?term=Hoppin%20JA%5BAuthor%5D&cauthor=true&cauthor_uid=27285288)2, [DeRoos AJ](https://www.ncbi.nlm.nih.gov/pubmed/?term=DeRoos%20AJ%5BAuthor%5D&cauthor=true&cauthor_uid=27285288)3, [Costenbader KH](https://www.ncbi.nlm.nih.gov/pubmed/?term=Costenbader%20KH%5BAuthor%5D&cauthor=true&cauthor_uid=27285288)4, [Alavanja MC](https://www.ncbi.nlm.nih.gov/pubmed/?term=Alavanja%20MC%5BAuthor%5D&cauthor=true&cauthor_uid=27285288)5, [Sandler DP](https://www.ncbi.nlm.nih.gov/pubmed/?term=Sandler%20DP%5BAuthor%5D&cauthor=true&cauthor_uid=27285288)1.

### Abstract

#### BACKGROUND:

Farming has been associated with rheumatoid arthritis (RA), but the role of pesticides is not known.

#### OBJECTIVES:

We examined associations between RA and pesticides or other agricultural exposures among female spouses of licensed pesticide applicators in the Agricultural Health Study.

#### METHODS:

Women were enrolled 1993-1997 and followed through 2010. Cases (N=275 total, 132 incident), confirmed by a physician or by self-reported use of disease modifying anti-rheumatic drugs), were compared with non-cases (N=24,018). Odds ratios (OR) and 95% Confidence Intervals (CI) were estimated using logistic regression models adjusted for age, state and smoking pack-years.

#### RESULTS:

Overall, women with RA were somewhat more likely to have reported lifetime use of any specific pesticide versus no pesticides (OR=1.4; 95%CI 1.0, 1.6). Of 15 pesticides examined, maneb/mancozeb (OR=3.3; 95%CI 1.5, 7.1) and glyphosate (OR=1.4; 95%CI 1.0, 2.1) were associated with incident RA compared with no pesticide use. An elevated, but non-statistically significant association with incident RA was seen for DDT (OR=1.9; 95%CI 0.97, 3.6). Incident RA was also associated with the application of chemical fertilizers (OR=1.7; 95%CI 1.1, 2.7) and cleaning with solvents (OR=1.6; 95%CI 1.1, 2.4), but inversely associated with lifetime livestock exposure as a child and adult (OR=0.48; 95%CI 0.24, 0.97) compared with no livestock exposure.

#### CONCLUSIONS:

Our results suggest that specific agricultural pesticides, solvents and chemical fertilizers may increase risk of RA in women, while exposures involving animal contact may be protective.

PMID: [27285288](https://www.ncbi.nlm.nih.gov/pubmed/27285288) DOI: [10.1289/EHP129](https://dx.doi.org/10.1289/EHP129)

An INVITRO abstract:

[PLoS One.](https://www.ncbi.nlm.nih.gov/pubmed/27280764" \o "PloS one.) 2016 Jun 9;11(6):e0156946. doi: 10.1371/journal.pone.0156946. eCollection 2016.

# The Impact of Glyphosate, Its Metabolites and Impurities on Viability, ATP Level and Morphological changes in Human Peripheral Blood Mononuclear Cells.

[Kwiatkowska M](https://www.ncbi.nlm.nih.gov/pubmed/?term=Kwiatkowska%20M%5BAuthor%5D&cauthor=true&cauthor_uid=27280764)1, [Jarosiewicz P](https://www.ncbi.nlm.nih.gov/pubmed/?term=Jarosiewicz%20P%5BAuthor%5D&cauthor=true&cauthor_uid=27280764)1, [Michałowicz J](https://www.ncbi.nlm.nih.gov/pubmed/?term=Micha%C5%82owicz%20J%5BAuthor%5D&cauthor=true&cauthor_uid=27280764)1, [Koter-Michalak M](https://www.ncbi.nlm.nih.gov/pubmed/?term=Koter-Michalak%20M%5BAuthor%5D&cauthor=true&cauthor_uid=27280764)1, [Huras B](https://www.ncbi.nlm.nih.gov/pubmed/?term=Huras%20B%5BAuthor%5D&cauthor=true&cauthor_uid=27280764)2, [Bukowska B](https://www.ncbi.nlm.nih.gov/pubmed/?term=Bukowska%20B%5BAuthor%5D&cauthor=true&cauthor_uid=27280764)1.

### [Author information](https://www.ncbi.nlm.nih.gov/pubmed/27280764" \o "Open/close author information list)

### Abstract

The toxicity of herbicides to animals and human is an issue of worldwide concern. The present study has been undertaken to assess toxic effect of widely used pesticide-glyphosate, its metabolites: aminomethylphosphonic acid (AMPA) and methylphosphonic acid and its impurities: N-(phosphonomethyl)iminodiacetic acid (PMIDA), N-methylglyphosate, hydroxymethylphosphonic acid and bis-(phosphonomethyl)amine on human peripheral blood mononuclear cells (PBMCs). We have evaluated the effect of those compounds on viability, ATP level, size (FSC-A parameter) and granulation (SSC-A parameter) of the cells studied. Human peripheral blood mononuclear cells were exposed to different concentrations of glyphosate, its metabolites and impurities (0.01-10 mM) for 4 and 24 h. It was found that investigated compounds caused statistically significant decrease in viability and ATP level of PBMCs. The strongest changes in cell viability and ATP level were observed after 24 h incubation of PBMCs with bis-(phosphonomethyl)amine, and particularly PMIDA. Moreover, all studied compounds changed cell granularity, while PMIDA and bis-(phosphonomethyl)amine altered PBMCs size. It may be concluded that bis-(phosphonomethyl)amine, and PMIDA caused a slightly stronger damage to PBMCs than did glyphosate. Changes in the parameters studied in PBMCs were observed only at high concentrations of the compounds examined, which clearly shows that they may occur in this cell type only as a result of acute poisoning of human organism with these substances.

PMID: [27280764](https://www.ncbi.nlm.nih.gov/pubmed/27280764) PMCID: [PMC4900596](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4900596/) DOI [10.1371/journal.pone.0156946](https://dx.doi.org/10.1371/journal.pone.0156946)

Notes from client:

* Animal means an animal was the experimental unit, in vitro means the treatment happened in a dish (cells, tissues).
* Studies can have more than one tag as both animal and in vitro, e.g., ex vivo studies would be both
* Non-human/non-animal studies with non-health based outcome that included laboratory equipment marked as not relevant
* Examples:
  + If a yeast cell/cell-line was used we recorded it in-vitro  
      
    Doostzadeh J,Davis RW,Giaever GN,Nislow C,Langston JW. Chemical genomic profiling for identifying intracellular targets of toxicants producing Parkinson's disease..#journal#. 2007/01//. 95:182
  + Also we considered studies in-vitro if they conducted a biochemical reaction with a relevant health endpoint such as antibody reaction or receptor binding

## Houz. 1-Methyl-4-phenylpyridinium (MPP+) does not exhibit paraquat-like immunoreactivity.. #journal#. 1990/10//. 53:339

Set all but ANIMAL aside for now. From each animal paper, annotate abstract and methods section.

**Sentence level annotation.**

The goal is to tag entire sentences that give certain kinds of information. Some sentences may have more than one tag. Some may have no tags.

**Funding:** Funding agency and grant number.

**Sex:**  must sometimes be inferred from words like *sow*, *ovary,* or *pregnant.*

* *Male and female SPF Hsd.Brl.Han Wistar rats (Toxi-Coop, Budapest, Hungary) were housed individually, with a 12-hour light-dark cycle at 19–25°C and 30–70% relative humidity, in type II polypropylene/polycarbonate cages with Lignocel® certified laboratory wood bedding.*
* *Fifty-four multiparous large white sows were used to determine the effects of supplementing oregano essential oil (OEO) to the gestation and lactation diets on oxidative stress status, lactation feed intake, and their piglet performance.*

**Strain:** (includes species)

* *Male and female SPF Hsd.Brl.Han Wistar rats (Toxi-Coop, Budapest, Hungary) were housed individually, with a 12-hour light-dark cycle at 19–25°C and 30–70% relative humidity, in type II polypropylene/polycarbonate cages with Lignocel® certified laboratory wood bedding.*
* *Thirty-five male and 35 female NIH Swiss Outbred mice (Harlan Laboratories, Indianapolis, IN, USA) weighing 15–20 g each were used.*

**AnimalSource:**

* *Twenty (20) adult male Sprague-Dawley rats of average weight 150 g were purchased from the Animal House Department of the Korle-Bu Teaching Hospital, Korle-Bu, Accra*
* *Male and female SPF Hsd.Brl.Han Wistar rats (Toxi-Coop, Budapest, Hungary) were housed individually, with a 12-hour light-dark cycle at 19–25°C and 30–70% relative humidity, in type II polypropylene/polycarbonate cages with Lignocel® certified laboratory wood bedding.*
* *Thirty-five male and 35 female NIH Swiss Outbred mice (Harlan Laboratories, Indianapolis, IN, USA) weighing 15–20 g each were used.*

**InitialAge:**

* *Twenty (20) adult male Sprague-Dawley rats of average weight 150 g were purchased from the Animal House Department of the Korle-Bu Teaching Hospital, Korle-Bu, Accra.*
* *At the start of the experimental period, animal­ were approximately seven weeks old and weighed 206–233 g (males) and 131–151 g (females).*
* *Two- to three-month-old Hsd:ICR male mice (28–35 g) were used in the experiments.*

**Husbandry**; This tag marks sentences that describe the general care and feeding of the laboratory animals. This include type of cage, feed, lab temperature, light/dark cycle,

* *All animal were treated in accordance with the guideline for the animal experiment of our laboratory which referred to the guidelines of Ministry of the Environment, Japan, Ministry of Health, Labour and Welfare, Japan, Ministry of Agriculture, Forestry and Fisheries, Japan, Ministry of Education, Culture, Sports, Science and Technology, Japan*
* *Male and female SPF Hsd.Brl.Han Wistar rats (Toxi-Coop, Budapest, Hungary) were housed individually, with a 12-hour light-dark cycle at 19–25°C and 30–70% relative humidity, in type II polypropylene/polycarbonate cages with Lignocel® certified laboratory wood bedding. Cages were 22 cm (width) by 32 cm (length) by 19 cm (height), and cages and bedding were changed weekly.*
* *Animals received ssniff® SM R/M-Z+H complete diet for rats and mice and potable tap water ad libitum.*
* *The rats were acclimatized to laboratory environment (20–24°C), % humidity with a 12 h light-darkness cycle for 7 days prior to experimentation. The rats had access to standard laboratory diet and water ad libitum. The experimental procedures were approved by the departmental ethical and protocol review committee and the Noguchi Memorial Institute for Medical Research Institutional Animal Care and Use Committee with protocol number 2013-01-3E and also conducted in accordance with international ethical guidelines.*

**Chemical:** The chemical or drug whose toxicity is being studied.

* *Synthetic 1,3,7,9-tetramethyluric acid (CAS number 2309-49-1; ≥98% pure as measured by high performance liquid chromatography (HPLC), proton nuclear magnetic resonance, and liquid chromatography-mass spectrometry methodologies) was supplied as the branded product TeaCrine® for use as the test article by its manufacturer (Compound Solutions, Inc., Carlsbad, CA).*
* *Sodium arsenite (99.6% purity) was acquired from J.T. Baker (Phillipsburg, NJ, USA)*
* *The following chemical and reagent tests were obtained from Sigma Chemicals Co. (St. Louis, MO, USA): V2O5(CAS number 1314-62-1), acridine orange (AO) (CAS number 10127-02-3), ethidium bromide (EB) (CAS number 1239-45-8), α-tocopherol (α-TOH) (CAS number 10127-02-3), and ascorbic acid (AA) (CAS number 50-81-7).*

**ChemSource:** The supplier of the test substance.

* *Five doses of L-BMAA (supplied by the Institute for Ethnomedicine, Jackson Hole, WY, USA) were prepared in sterile water and adjusted to pH 6.5 with NaOH [*[*1*](https://www.hindawi.com/journals/jt/2015/739746/#B1)*] prior to IP injection.*
* *Sodium arsenite (99.6% purity) was acquired from J.T. Baker (Phillipsburg, NJ, USA)*

**ChemPurity:**

* *Sodium arsenite (99.6% purity) was acquired from J.T. Baker (Phillipsburg, NJ, USA)*
* *Synthetic 1,3,7,9-tetramethyluric acid (CAS number 2309-49-1; ≥98% pure as measured by high performance liquid chromatography (HPLC), proton nuclear magnetic resonance, and liquid chromatography-mass spectrometry*

**DoseLevel:** Ideally given in mg/kg/day, but may be given simply in mg or mL.

* *The dose levels of theacrine utilized in the study were 375, 300, and 180 mg/kg bw/day.*
* *Each dose was dissolved in 0.5 mL of sterile H2O and calculated as follows depending on each mouse weight: Dose (mg/g BW) × mouse weight (15–20 g) = Y mg/mouse (L-BMAA/mouse), for example, Group E Dose (3 mg/g BW) × 18 g = 54 mg/0.5 mL.*

**Vehicle:** This is the substance in which the test substance is dissolved or mixed for administration.

* *The test article doses were prepared by suspending theacrine in 1% aqueous methylcellulose to achieve concentrations of 18, 30, and 37.5 mg/mL in order to provide a constant dosing volume of 10 mL/kg bw.*
* *Five doses of L-BMAA (supplied by the Institute for Ethnomedicine, Jackson Hole, WY, USA) were prepared in sterile water and adjusted to pH 6.5 with NaOH [*[*1*](https://www.hindawi.com/journals/jt/2015/739746/#B1)*] prior to IP injection.*
* *The corn oil (delivery vehicle for fat-soluble compounds) also was obtained from Sigma Chemicals Co. (CAS number 8001-30-7).*
* *Groups of five Hsd:ICR mice were treated with the following: (a) vehicle, distilled water; (b) vehicle, corn oil; (c) AA, 100 mg/kg intraperitoneally (ip); (d) α-TOH, 20 mg/kg by gavage; (e) V2O5, 40 mg/kg by ip injection; (f) AA + V2O5; and (g) α-TOH + V2O5.*

**Route:** Route of administration: gavage, IV, intratracheal, sub-q, etc.

* *Five doses of L-BMAA (supplied by the Institute for Ethnomedicine, Jackson Hole, WY, USA) were prepared in sterile water and adjusted to pH 6.5 with NaOH [*[*1*](https://www.hindawi.com/journals/jt/2015/739746/#B1)*] prior to IP injection.*
* *Groups of five Hsd:ICR mice were treated with the following: (a) vehicle, distilled water; (b) vehicle, corn oil; (c) AA, 100 mg/kg intraperitoneally (ip); (d) α-TOH, 20 mg/kg by gavage; (e) V2O5, 40 mg/kg by ip injection; (f) AA + V2O5; and (g) α-TOH + V2O5.*
* *On the sixth day, animals received a subcutaneous injection of sterile carrageenan solution (1%; 1 mL).*

**StudyDesign:** Words like acute, subacute, chronic, developmental may be used, or a testing guideline such as OECD 408 maybe mentioned.

* *The 90-day study was conducted according to OECD GLP (ENV/MC/CHEM (98)17; OECD, Paris, 1998) and in compliance with OECD 408 (adopted 21st September 1998; 90-day study) [*[*27*](https://www.hindawi.com/journals/jt/2016/6206859/#B27)*] and US FDA Redbook 2000, IV.C.4.a (2003; 90-day study) guidelines [*[*28*](https://www.hindawi.com/journals/jt/2016/6206859/#B28)*].*
* *Fifteen mice per group received 0.5 or 5.0 mg As/L of DW for six months.* (From the length of the study, we infer that it is a *chronic* study.)
* *The aim of our study was to assess the effect of subchronic (28-fold) administration of a 50% ethanol extract of MO leaves (200 mg/kg, p.o.) compared with rosmarinic acid (RA, 10 mg/kg, p.o.) and huperzine A (HU, 0.5 mg/kg, p.o.) on behavioral and cognitive responses in scopolamine-induced rats.*

**StudySize:** Any sentence that tells the number of subjects in an arm of the study or the entire study:

* *Both groups contained ten (10) rats each.*
* *Fifteen mice per group received 0.5 or 5.0 mg As/L of DW for six months.*
* *Thirty-five male and 35 female NIH Swiss Outbred mice (Harlan Laboratories, Indianapolis, IN, USA) weighing 15–20 g each were used.*

**Allocation:** (randomization, allocation concealment, blinding)

* *The Sprague-Dawley rats were randomly assigned to the experimental group and the control group for 7 days before the start of the experiment.*
* *Eighty male and female rats were stratified by body weight and randomly assigned to four dose groups containing 10 rats/sex/group.*

**NegControls:** (Placebo treated? No treatment? )

* Group I (DW): Served as the control and were administered 2 ml/kg of distilled water daily
* The control group received distilled water, while the test groups received either 50 or 500 mg/kg body weight of Roundup® diluted in distilled water.
* We divided 50 Wistar rats into five following groups (n=10 per group): i. Control-intact animals, ii. Vehicle-phosphate buffered saline (PBS) injection into the vas deferens, iii. KRG-an intraperitoneal (IP) injection of KRG, iv. EO-an injection of uropathogenic Escherichia coli (UPEC) strain M39 into the vas defer- ens, and v. EO/ KRG-injections of both UPEC strain M39 and KRG.

**PosControls:** (expected response?)

**EndPoint:** (e.g., infertility)

* Acute EO increased the relative weight of prostate and seminal vesicles (P≤0.05). It also reduced sperm quality such as total motility, sperm concentration (P≤0.01), and the percentage of normal sperm (P≤0.001).

**EndPointCat:**

Tag entire sentence as “EndpointCategory”. Some health categories include:

* Cancer
* Cardiovascular System
* Congenital, Hereditary and Neonatal
* Endocrine System
* Gastrointestinal System
* Hematological and Immune System
* Hepatic System
* Mood and Mental Disorders
* Musculoskeletal System
* Nervous System
* Nutritional and Metabolic
* Ocular and Sensory
* Renal
* Reproductive and Developmental
* Respiratory Tract
* Skin and Connective Tissue

**StatMethods:** Any sentence describing statistical methods or software (SAS, etc.)

* *Statistical analyses were conducted using SPSS PC+ software (SPSS, Inc., Chicago, IL). Bartlett’s homogeneity of variance test was used to assess heterogeneity of variance between groups and was followed by a one-way analysis of variance (ANOVA) if no significant heterogeneity was detected. Duncan’s Multiple Range test was used to assess the significance of intergroup differences if a positive ANOVA result was obtained. Where significant heterogeneity was detected by Bartlett’s test, the Kolmogorov-Smirnov test was performed to examine normally distributed data, and Kruskal-Wallis nonparametric one-way ANOVA, followed by the Mann-Whitney U test for intergroup comparisons of positive results, was used in the case of a nonnormal distribution. A p value of <0.05 was considered statistically significant, and statistically significant results were reported at  and  levels.*
* *Statistical significance between groups was performed by applying analysis of one-way variance (ANOVA) followed by Dunnett’s and Bonferroni’s test using GraphPad Prism 5.0 software. p values less than 0.05 () were considered significant.*

*Client’s original description of fields (superset of above):*

|  |  |
| --- | --- |
| **ANIMAL** | |
| ***Funding*** | Funding source(s) |
| Reporting of COI by authors (\*reporting bias) |
| ***Animal Model*** | Sex |
| Species |
| Strain |
| Source of animals |
| Age or lifestage at start of dosing and at health outcome assessment |
| Diet and husbandry information (e.g., diet name/source) |
| ***Treatment*** | Chemical name and CAS number |
| Source of chemical |
| Purity of chemical (\*information bias) |
| Dose levels or concentration (as presented and converted to mg/kg bw/d when possible) |
| Other dose-related details, such as whether administered dose level was verified by measurement, information on internal dosimetry (\*information bias) |
| Vehicle used for exposed animals |
| Route of administration (e.g., oral, inhalation, dermal, injection) |
| Duration and frequency of dosing (e.g., hours, days, weeks when administration was ended, days per week) |
| ***Methods*** | Study design (e.g., single treatment, acute, subchronic (e.g., 90 days in a rodent), chronic, multigenerational, developmental, other) |
| Guideline compliance (i.e., use of EPA, OECD, NTP or another guideline for study design, conducted under GLP guideline conditions, non-GLP but consistent with guideline study, non-guideline peer-reviewed publication) |
| Number of animals per group (and dams per group in developmental studies) (\*missing data bias) |
| Randomization procedure, allocation concealment, blinding during outcome assessment (\*selection bias) |
| Method to control for litter effects in developmental studies (\*information bias) |
| Use of negative controls and whether controls were untreated, vehicle-treated, or both |
| Report on data from positive controls – was expected response observed? (\*information bias) |
| Endpoint health category (e.g., reproductive) |
| Endpoint (e.g., infertility) |
| Diagnostic or method to measure endpoint (\*information bias) |
| Statistical methods (\*information bias) |
| ***Results*** | Measures of effect at each dose or concentration level (e.g., mean, median, frequency, and measures of precision or variance) or description of qualitative results. When possible, OHAT will convert measures of effect to a common metric with associated 95% confidence intervals (CI). Most often, measures of effect for continuous data will be expressed as mean difference, standardized mean difference, and percent control response. Categorical data will be expressed as relative risk (RR, also called risk ratio). |
| No Observed Effect Level (NOEL), Lowest Observed Effect Level (LOEL), benchmark dose (BMD) analysis, statistical significance of other dose levels, or other estimates of effect presented in paper. **Note:** The NOEL and LOEL are highly influenced by study design, do not give any quantitative information about the relationship between dose and response, and can be subject to author’s interpretation (e.g., a statistically significant effect may not be considered biologically important). Also, a NOEL does not necessarily mean zero response. Ideally, the response rate at specific dose levels is used as the primary measure to characterize the response. |
| If not presented in the study, statistical power can be assessed during data extraction using an approach that assesses the ability to detect a 10% to 20% change from control group’s response for continuous data, or a relative risk or odds ratio of 1.5 to 2 for categorical data, using the outcome frequency in the control group to determine sample size. Recommended sample sizes to achieve 80% power for a given effect size, i.e., 10% or 20% change from control, will be compared to sample sizes used in the study to categorize statistical power. Studies will be considered adequately powered when sample size for 80% power is met. |
| Observations on dose response (e.g., trend analysis, description of whether dose-response shape appears to be monotonic, non-monotonic) |
| Data on internal concentration, toxicokinetics, or toxicodynamics (when reported) |
| ***Other*** | Documentation of author queries, use of digital rulers to estimate data values from figures, exposure unit, and statistical result conversions, etc. |