

# **Guideline For The Use Of Der/Xml Composer – Rat Metabolism v.5.2**

***Prepared for use with DER Composer, a product resulting from the joint cooperation between the U.S. Environmental Protection Agency (USEPA) and the Laboratory of Mathematical Chemistry (LMC-Bourgas, Bulgaria).***

The views expressed in this presentation are those of the authors and do not necessarily reflect the views or policies of the U.S. EPA.

# Part 1:

- **Opening DER Composer**
- **General info**
- **Material and methods**



Start with the tab **I. General info**. Begin by filling in pertinent information by mouse-clicking within the boxed areas designated for those parameters and typing information or by copying / pasting information from an electronic source down to the area to fill in citations.

\\AA.AD.EPA.GOV\ORD\DUL\USERS\rkolancz\Net MyDocuments\UnnamedDER.xml - DER Composer

DER Composer v5.2 (Rat/Livestock) ation with US EPA/ORD/NERL-NHEERL

**I. General info** | ~~II. Materials and methods~~ | ~~III. Results~~ | ~~IV. Discussion and conclusions~~ | ~~V. References~~

Header

**EPA REVIEWER:**   
[Insert Branch], Health Effects Division (7509C)

**EPA SECONDARY REVIEWER:**   
[Insert Branch], Health Effects Division (7509C)

**EPA WAM:**   
[Insert Branch], Health Effects Division (7509C)

**TXR#:**

**STUDY TYPE:** Metabolism rat; OPPTS 870.7485[85-1]; OECD 417

**AGENCY CODE:** US EPA PC CODE

Code type	Code value

**DP BARCODE:**

**SUBMISSION NO:**

**TEST MATERIAL COMMON NAME:**  Place common name (company experimental name) here

**TEST MATERIAL PURITY:**  %

**IUPAC NAME:**

Signature   
021

Signature   
021

Signature   
021

Start with the tab **I. General info**. Begin by filling in pertinent information by mouse-clicking within the boxed areas designated for those parameters and typing information or by copying / pasting information from an electronic source down to the area to fill in citations.

Skip Reviewer Section and USEPA Specific Fields for TXR#, DP Barcode & Submission No. Begin with Agency Code. Select from Drop-down Menu (CAS, EFSA, PC Code, etc...) or New Additional Code then Add with Red Arrow. Then Fill Appropriate Value.

Then Continue Filling Test Material Common Name, Test Material Purity, IUPAC Name, Synonyms, and End Use Products.



**A CITATION EDITOR box pops up. Fill in reference, MRID number and click generate tables, followed by clicking on submit. If there are additional references repeat the process - click the + to add each, populate, and click submit.**

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I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

**IUPAC NAME:** 2-[4-(Methylsulfonyl)-2-nitrobenzoyl]cyclohexane-1,3-dione

**SYNONYMS:** ZA1296;

**END-USE PRODUCT:**

**CITATION**

**Click on "+" to Open Citation Editor**

Reference	MRID
<input type="checkbox"/> (1996) ZA1296: Excretion and tissue retention of a single oral dose (100 mg/kg) in the rat. Central Toxicology La...	44505102
<input checked="" type="checkbox"/> (1996) ZA1296: Biotransformation in the rat. Central Toxicology Laboratory, Cheshire, UK. Laboratory Report/St...	44505103
<input type="checkbox"/> (1996) ZA1296: Excretion and tissue retention of a single oral dose (1 mg/kg) in the rat. Central Toxicology Labor...	44505104
<input type="checkbox"/> (1996) ZA1296: Excretion and tissue retention of a single intravenous dose (1 mg/kg) in the rat. Central Toxicolo...	44505105
<input type="checkbox"/> (1996) ZA. 1296: Excretion and tissue retention of a single oral dose (1 mg/kg) in the rat following repeat dosing. ...	44505106

**SPONSOR:** Zeneca Ag Products, Wilmington, DE 19850-5458

**EXECUTIVE SUMMARY**

In a series of rat metabolism studies (MRIDs 44505101 through 44505106), [14C-aromatic]mesotrione (98.1% radiochemical pur... at 1.00 mg/kg following a 14-day pretreatment with mesotrione at 1.00 mg/kg/day. In addition, 2 bile-duct cannulated rats/sex v...

The overall recovery of dosed radioactivity in excreta, bile, tissues, cage washes was 72.0-97.1% from rats in the mass balance 54.2-55.9% of the dose in the urine and 2.3.8-24.5% of the dose in the feces. Radioactivity remaining in the carcass/issues of the majority of the dose in the urine (61.5-63.0% dose), with fecal excretion accounting for 28.8-30.5% dose, although the rec...

**COMPLIANCE**

Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

**Citations Editor**

Reference  
(1996) ZA1296: Biotransformation in the rat. Central Toxicology Laboratory, Cheshire

MRID  
44505103

☒ Generate Tables for this reference

Submit Cancel

**Fill-in Citation, MRID if associated with USEPA, and make sure Generate Table for Reference Box is Checked.**

**Fill-in Executive Summary & Compliance Text Boxes.**

**The citation is entered and tables are created and are ready for population. Additional references (MRID's) may be entered by repeat of the afore mentioned process**

Next the tab **II. Materials and methods** and sub-tab **A. Materials** may be populated. Data is filled in via directly typing or copy/paste from electronic documents until reaching the structure entry. To enter the **Radio-labeled Test Material** and **Non-radio-labeled Test Material** structures:

\\AA.AD.EPA.GOV\ORD\DUL\USERS\rkolancz\Net MyDocuments\UnnamedDER.xml - DER Composer

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**II. Materials and Methods section**

I. General info | **II. Materials and methods** | III. Results | IV. Discussion and conclusions | V. Appendix | VI. Attachments

A. Materials | B. Study design and methods

**1. Test Compound**

Radio-labeled test material

ADD DEL


**Radio-labeled test material:** Indicate site of label in brackets followed by common name and company experimental name in parenthesis

Radio-labeled #1

**Radio-labeled purity:**  %

**Specific activity:**  units

**Lot/batch #:**



**Structure:**

Non-Radio-labeled test material

**Non-radio-labeled test material:** Use common name with company experimental name in parenthesis

**Description:**

**Lot/batch #:**

**Purity:**  %

**Contaminants:**

**CAS # of TGAI:**

Fill Common Name w/ Radio-label & Location  
Add Purity, Specific Activity, Lot/Batch

Click on Icon to Open 2D Structure Editor

Below is a graphic of the **STRUCTURE DRAWING** editor pop-up box. The large white area is the drawing workspace, the **light-blue box** is where a SMILES string may be entered or displayed, and the **yellow box** is where a CAS number can be entered. Scrolling over the top of the icons will give some indication of their utility.

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2D Editor

SMILES/InChi

000000-00-0

Template Work Common Fragments

Radio-labeled test material

Radio-labeled #1

Non-Radio-labeled test material

Non-radio-labeled test material:

Description:

Lot/batch #:

Purity:

Contaminants:

CAS # of TGA:

drag the mouse with left button pressed to create bond

OK Cancel

oasis-lmc.org

**SMILES String**

**CAS Number**

Option to Fill-in Structure by Pasting SMILES String in Blue Box or By Use of the Drawing Tools. Will Eventually Need Modification of SMILES to Capture Radio-Label Information.w2


To get started a good source of parent nomenclature, 2-D structures represented as linear “SMILES strings”, etc are available on the Pesticide Properties DataBase (PPDB) of the University of Hertfordshire web-site.

<http://sitem.herts.ac.uk/aeru/ppdb/en/index.htm>


Remote Access Sign On | One EP: x Metrafenone (Ref: BAS 560F) x +

← → ↻ ⚠ Not secure | sitem.herts.ac.uk/aeru/ppdb/en/Reports/468.htm


# PPDB: Pesticide Properties DataBase

University of Hertfordshire 

Home Top Environmental Fate Ecotoxicology Human Health Translations

A to Z: All  
A to Z: Insecticides  
A to Z: Herbicides  
A to Z: Fungicides  
A to Z: Other product constituents  
Search  
Support information  
Purchasing and licensing  
 Find us on: facebook


**Metrafenone (Ref: BAS 560F)**  
(Also known as: AC 375839)

Last updated: 22/02/2021 

## GENERAL INFORMATION

Description	A fungicide used to control disease on cereals and other crops
Example pests controlled	Powdery mildew; Eyespot; Ear blight; Rusts
Example applications	Wheat; Barley; Oats; Rye; Triticale; Grapes
Efficacy & activity	Wheat/Eyespot=Moderate; Wheat/Mildew=High; Wheat/Septoria tritici/Low; Mildew=Moderate for protection, Low for eradication
Availability status	Current
Introduction & key dates	2006

### UK regulatory status

UK COPR regulatory status 	Approved
Date COPR inclusion expires	30/04/2024
UK LERAP status	None

### EC Regulation 1107/2009 (repealing 91/414)

EC Regulation 1107/2009 status	Approved
Dossier rapporteur/co-rapporteur	Latvia/Slovakia
Date EC 1107/2009 inclusion expires	30/04/2021

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ALSO AVAILABLE: THE VSDB THE BPDB

www.herts.ac.uk/aeru

11:37 AM 4/13/2021



Perform a right-hand click of the mouse in the light-blue box of the **STRUCTURE DRAWING** package and select paste to enter the parent structure.

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2D Editor

SMILES/InChi CS(=O)(=O)c1ccc(C(=O)C2C(=O)CCCC2=O)c(N(=O)=O)c1

000000-00-0

Templates Work Common Fragments

Radio-labeled test material

ADD DEL

Radio-labeled #1

Non-Radio-labeled test material

Non-radio-labeled test material:

Description: drag the mouse with left button pressed to create bond

Lot/batch #:

Purity:

OK Cancel

As the SMILES string is pasted within the blue-box, a 2-D structure appears below in the white structure display box.

The parent structure (now present in the **STRUCTURE DRAWING** editor) may be modified utilizing tools within the editor. Specifically a label may be introduced in the structure of the radio-labeled parent.

# Radio labeling of atoms

Within the STRUCTURE DRAWING window, open the periodic table by selecting the icon as circled in the figure below.

DER Composer v5.2 (Rat/Livestock)  
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2D Editor

SMILES/InChi: CS(=O)(=O)c1ccc(C(=O)C2C(=O)CCCC2=O)c(N(=O)=O)c1

000000-00-0

Templates Work Common Fragments

Radio-labeled test material

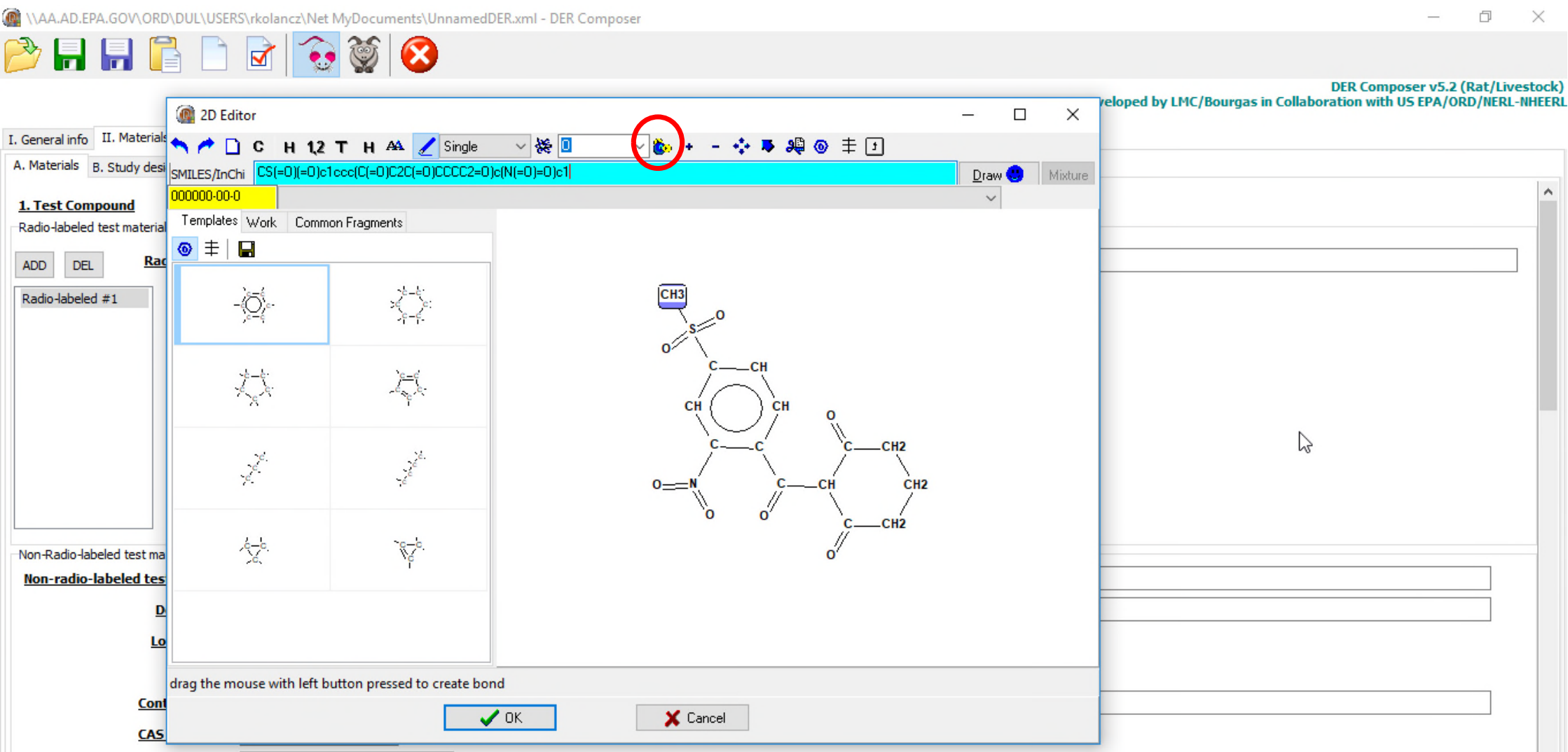
Radio-labeled #1

Non-Radio-labeled test material

Non-radio-labeled test material

drag the mouse with left button pressed to create bond

OK Cancel



A periodic table screen comes up where you should check labeled, in this example add 14 in the number box and click on C for carbon. Then hit YES.

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2D Editor

I. General info II. Materials

A. Materials B. Study design

SMILES/InChi CS(=O)(=O)c1ccc(O)cc1

000000-00-0

Templates Work Common Fra

1. Test Compound

Radio-labeled test material

ADD DEL Rad

Radio-labeled #1

Non-Radio-labeled test material

Non-radio-labeled test material

drag the mouse with left button

Periodic Table

1 H																	2 He														
3 Li	4 Be																	5 B	6 C	7 N	8 O	9 F	10 Ne								
11 Na	12 Mg																	13 Al	14 Si	15 P	16 S	17 Cl	18 Ar								
19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr														
37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe														
55 Cs	56 Ba	57 *La	72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 Pt	79 Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rn														
87 Fr	88 Ra	89 *Ac																													
																		58 Ce	59 Pr	60 Nd	61 Pm	62 Sm	63 Eu	64 Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb	71 Lu
																		90 Th	91 Pa	92 U	93 Np	94 Pu	95 Am	96 Cm	97 Bk	98 Cf	99 Es	100 Fm	101 Md	102 No	103 Lr

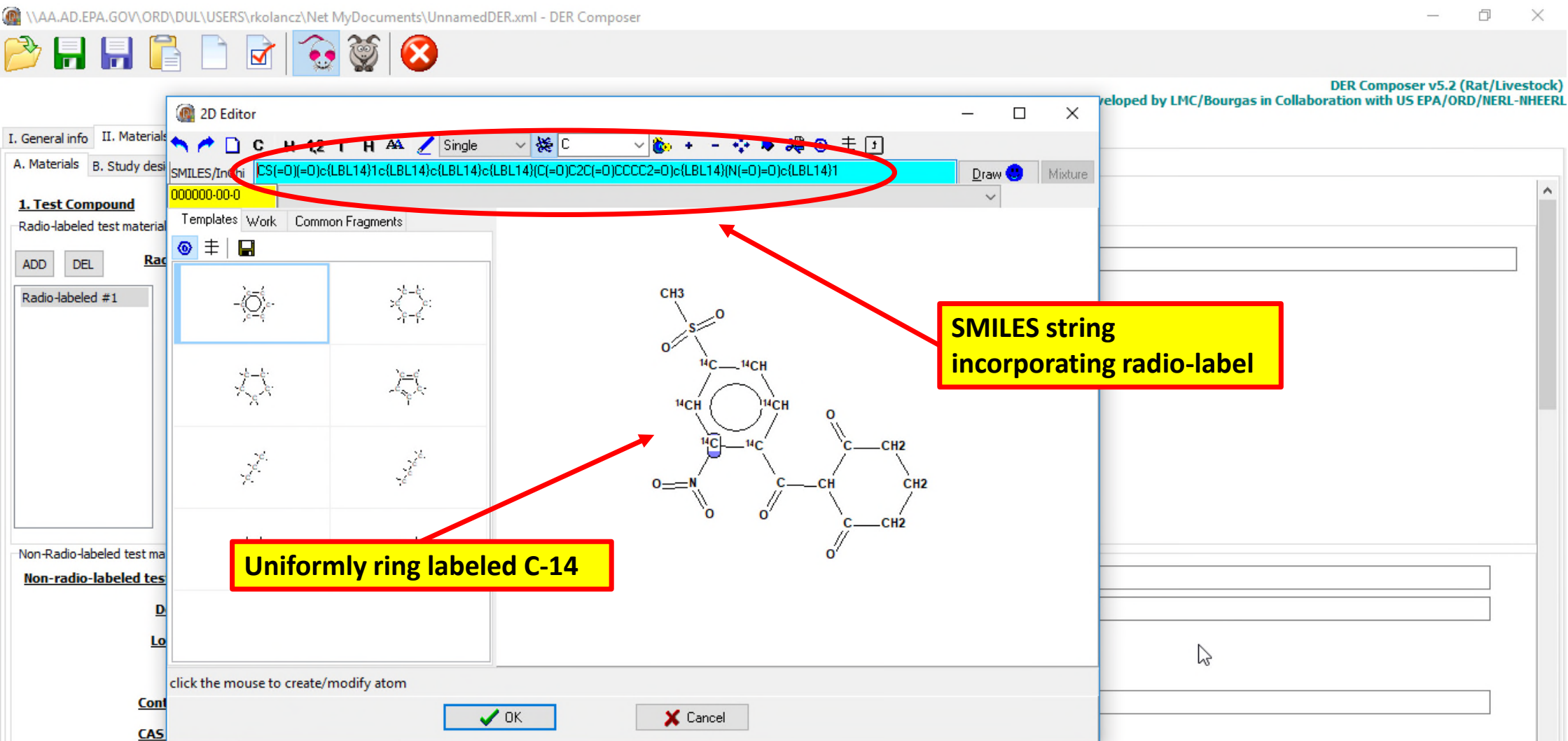
Selected element: C{LBL14}

☒ Labeled

Number: 14

Yes Cancel Help

After clicking Yes on the previous screen, the periodic table closes, then you can add the C-14 label to each carbon in the example. The example below happens to be a uniformly labeled phenyl ring. Note that the information for the labeling is now contained in the SMILES.





I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

A. Materials B. Study design and methods

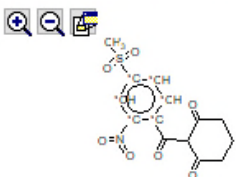
ADD DEL **Radio-labeled test material:** Mesotrione [14C-aromatic]

**Radio-labeled #1**

**Radio-labeled purity:** 97 %

**Specific activity:** 1.12-1 GBq/mmol

**Lot/batch #:** Y06684/159 or Y06684/011

**Structure:** 

Note: 2-D Structure with Radio-label. Fill Test Material Including Common Name with Radio-label Site, Purity, Specific Activity, and Lot/Batch.

Non-Radio-labeled test material

**Non-radio-labeled test material:** Use common name with company experimental name in parenthesis

**Description:**

**Lot/batch #:**

**Purity:** %

**Contaminants:**

**CAS # of TGAI:**

Modified Rat

The Non-radiolabeled Test Material may be entered in the same fashion by opening the STRUCTURE DRAWING PACKAGE.

\\AA.AD.EPA.GOV\ORD\DUL\USERS\rkolancz\Net MyDocuments\UnnamedDER.xml - DER Composer

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I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

A. Materials B. Study design and methods

Lot/batch #: Y06684/159 or Y06684/U11

Structure:

Non-Radio-labeled test material

Non-radio-labeled test material: Use common name with company experimental name in parenthesis

Description:

Lot/batch #:

Purity: %

Contaminants:

CAS # of TGA:

Structure:

Click icon to open STRUCTURE DRAWING window

The SMILES string (from the excel list of parent structures) is entered in the light-blue box of the editor and the 2-D structure is immediately shown.

**NOTE:** The use of COPY/PASTE SMILES strings to generate the 2-D structures of parent chemicals serves to save time drawing structures, however the structures can be produced utilizing the tools of the drawing package.

DER Composer v5.2 (Rat/Livestock) C/Bourgas in Collaboration with US EPA/ORD/NERL-NHEERL

DER Composer

2D Editor

SMILES/InChi CS(=O)(=O)c1ccc(C(=O)C2C(=O)CCCC2=O)c(N(=O)=O)c1 Draw Mixture

Lot/batch 000000-00-0

Templates Work Common Fragments

click/drag with: left button to select; right button to move

OK Cancel

DER Composer v5.2 (Rat/Livestock) C/Bourgas in Collaboration with US EPA/ORD/NERL-NHEERL

I. General info II. Materials and methods III. Results

A. Materials B. Study design and methods

Non-Radio-labeled test material

**Non-radio-labeled test material:** Use common

Description:

Lot/batch #:

Purity: %

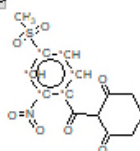
Contaminants:

CAS # of TGA:

I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

A. Materials B. Study design and methods

Lot/batch #: Y06684/159 or Y06684/U11



Structure:

Non-Radio-labeled test material

Non-radio-labeled test material: Mesotrione

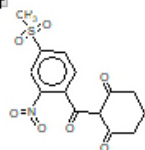
Description: Cream solid or off-white powder

Lot/batch #: Y06684/008 or Y06684/005

Purity: >99.3 %

Contaminants: not specified

CAS # of TGA1: 104206-82-8



Structure:

Physicochemical Properties

Parameter	Note	Value	Reference
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Modified	Rat
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Note: 2-D Structure for Non-radio-label Test Material. Finish Filling Test Material Including Common Name, Description of Material, Lot/Batch, Purity, Any Contaminants, and CAS #.

Continue filling out the rest of **II. Material and methods A. Materials**

C:\Users\rkolancz\0\_Working Files\MetaPath Users Group\EFSA Contract\Mesotrione.xml - DER Composer

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I. General info

II. Materials and methods

III. Results

IV. Discussion and conclusions

V. Appendix

VI. Attachments

A. Materials

B. Study design and methods

3. Test animals

Species: Rat

Strain: Alpk:APISD

Age at study initiation: 7-9 weeks

Weight at study initiation: 175-300 g

Source: Biological Services Section or Barrired Animal Breeding Unit, Zeneca Pharmaceuticals, Alderley Park

Housing: During initial acclimation, rats were housed in groups of the same sex in s ock rat cages. During the in-life p

Diet: Pelleted PCD rat diet (Special Diet Services, Ltd, Stepfield, Wiltham. Essex. UK). ad libitum, except for 10-:

Water: Tap water, ad libitum

Environmental conditions

Temperature: 21 ± 4 °C

Humidity: 30-70%

Air changes: At least 12/hour

Photoperiod: 12-hr photoperiod

Acclimation period: 4 days

4. Preparation of dosing solutions

For the low-udose groups, undiluted [14C-aromatic] mesotrione was dissolved in sodium bicarbonate solution. The composition of the final dosing solution was 0.25 mg mesotrione/g and 1.04 MBq/g of dosing solution. For the high-dose groups, [14C-aromatic]mesotrione was dissolved in sodium bicarbonate solution and isotopically diluted by mixing with non-labeled mesotrione. The final specific activity of the dosing solution was 4.19MBq/mg for the low-dose groups and 65.31 KBq/mg for the high-dose groups. Following dosing; the radiochemical purity of the test substance was determined by HPLC analysis; for the biliary study, the purity was determined using TLC and silica gel column chromatography. No results of these analyses were provided.

Fill-in Test Animal Fields

Fill-in Preparation of Dosing Solution

# Go To Live Demo

C:\Users\rkolancz\Documents\UnnamedDER.xml - DER Composer

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I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

**EPA SECONDARY REVIEWER:**  *Signature*   
[Insert Branch], Health Effects Division (7509C) **DATE:** 4/13/2021

**EPA WAM:**  *Signature*   
[Insert Branch], Health Effects Division (7509C) **DATE:** 4/13/2021

**TXR#:**

**DATA EVALUATION RECORD**

**STUDY TYPE:** Metabolism rat; OPPTS 870.7485[85-1]; OECD 417

**AGENCY CODE:** US EPA PC CODE

Code type	Code value

**DP BARCODE:**

**SUBMISSION NO.:**

**TEST MATERIAL COMMON NAME:** Place common name (company experimental name) here

**TEST MATERIAL PURITY:**  %

**IUPAC NAME:**

**SYNONYMS:**

**END-USE PRODUCT:**

**CITATION**  
+

Reference	MRID

Rat

11:24 AM  
4/13/2021

Questions ???  
&  
Answers

## Part 2:

- **Appendix 1**
- **Appendix 2**
- **Material and methods**
- **Study design**



Next go to tab **V. Appendix** – It is within this section that the various treatment groups are defined and listed as a **TEST** in the appendix 1 table below. A treatment group may be defined by gender, age, dose amount, dose route, sample matrix or other experimental descriptor (parameters that when varied may give rise to a different metabolic map for a particular chemical).

C:\Users\rkolancz\0\_Working Files\Metabolism Data Curation\Open Lit\_Cross Reference\170\_Mesotrione\_Rat\Mesotrione.xml - DER Composer

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I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

Appendix1a

+ [icon] [icon]

Test#	Number	Dose Route	Dose (nominal)	Dose (measured)	Dose Type	Test Duration	Matrix	Experimental Descriptor	Remarks

A test group is entered by clicking on the + icon to bring up an editor box.

Appendix2

+ [icon] [icon] [icon] Tree List [icon]

ID	Common Name / Code	Chemical Name	SMILES	Parent(s)	Expertise
----	--------------------	---------------	--------	-----------	-----------

Rat

Windows taskbar: 12:33 PM 2/16/2021

I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

Appendix1a



Test#	Sex	Number	Dose Route	Dose (nominal)	Dose (measured)	Dose Type	Test Duration	Matrix	Experimental Descriptor	Remarks

**Appendix1 Editor**

Test#  
1A

Gender  
☒ Male
 ☐ Female
 ☐ Not Reported

Number  
5

Dose Route  
Oral

Dose Nominal  
100 mg/kg

Dose Measured  
100.11 mg/kg

Matrix  
Urine

Test Duration  
72 hrs

Experimental Descriptor

Dose Type  
☒ Single
 ☐ Multiple  
 on every:    
 for:

Remarks  
 sed for metabolite identification and characterization

Submit Cancel

Appendix 1 Editor box – example filled in

Appendix2



ID Common Name / Code Chemical Name

Rat

Click on submit to accept test – continue to add new tests via the same process until completed. Screen should appear as below:

C:\Users\rkolancz\0\_Working Files\Metabolism Data Curation\Open Lit\_Cross Reference\170\_Mesotrione\_Rat\Mesotrione.xml - DER Composer

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I. General infoII. Materials and methodsIII. ResultsIV. Discussion and conclusionsV. AppendixVI. Attachments

+ | | | |

Test#	Sex	Number	Dose Route	Dose (nominal)	Dose (measured)	Dose Type	Test Duration	Matrix	Experimental Descriptor	Remarks
10A	Female	2	Oral	50.0 mg/kg	48.5 mg/kg	single	48 hrs	Urine		pooled samples of feces, urine, and bil
10B	Female	2	Oral	50.0 mg/kg	48.5 mg/kg	single	48 hrs	Feces		pooled samples of feces, urine, and bil
10C	Female	2	Oral	50.0 mg/kg	48.5 mg/kg	single	48 hrs	Bile		pooled samples of feces, urine, and bil
11A	Male	2	Oral	100.0 mg/kg	104.8 mg/kg	single	48 hrs	Urine		used solely as a source of fecal and ur
11B	Male	2	Oral	100.0 mg/kg	104.8 mg/kg	single	48 hrs	Feces		used solely as a source of fecal and ur
12A	Female	2	Oral	100.0 mg/kg	110.7 mg/kg	single	48 hrs	Urine		used solely as a source of fecal and ur
12B	Female	2	Oral	100.0 mg/kg	110.7 mg/kg	single	48 hrs	Feces		used solely as a source of fecal and ur

Appendix2

+ | | | |










Tree

List

ID	Common Name / Code	Chemical Name	SMILES	Parent(s)	Expertise
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The completed **Appendix 1** will automatically populate the [group arrangements](#) **Table 1** of section/tab **II. Materials and methods** sub-tab **B. Study design and methods**. This may be observed by clicking on the appropriate tabs.

C:\Users\rkolancz\0\_Working Files\Metabolism Data Curation\Open Lit\_Cross Reference\170\_Mesotrione\_Rat\Mesotrione.xml - DER Composer



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I. General infoII. Materials and methodsIII. ResultsIV. Discussion and conclusionsV. AppendixVI. Attachments

A. MaterialsB. Study design and methods

1. Group arrangements

Animals were assigned to the test groups noted in Table 1

Table 1a

Treatment Group	Sex	Number	Dose Route	Dose (nominal)	Dose (measured)	Dose Type	Remarks
1	Mal	5	Oral	100mg/kg	100.11mg/kg	single	Feces,Tissue
2	Fer	5	Oral	100mg/kg	98.79mg/kg	single	Feces,Tissue
3	Mal	5	Oral	1.0mg/kg	1.0mg/kg	single	Feces,Tissue
4	Fer	5	Oral	1.0mg/kg	1.0mg/kg	single	Feces,Tissue
5	Mal	5	Oral	1.0mg/kg	0.99mg/kg	multiple	Feces,Tissue
6	Fer	5	Oral	1.0mg/kg	1.02mg/kg	multiple	Feces,Tissue
7	Mal	5	I.V.	1.0mg/kg	0.99mg/kg	single	Feces,Tissue

2. Dosing and sample collection

Briefly describe dosing methods and sample collection

Table 2a

Treatment Group	Matrix	Sample Time	Major Method	Conjugate Analysis	Analytical Separation	Analytical Detection	Remarks
-----------------	--------	-------------	--------------	--------------------	-----------------------	----------------------	---------

**In addition, an automatic partial entry of the dosing and sample collection Table 2 of section/tab II. Materials and methods sub-tab B. Study design and methods takes place. We will return to complete this table after completion of Appendix 2.**

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I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

A. Materials B. Study design and methods

Table 2a

Treatment Group	Matrix	Sample Time	Major Method	Conjugate Analysis	Analytical Separation	Analytical Detection	Remarks
10A, 11A, 12A, 1A, 2A	Urine						
10B, 11B, 12B, 1B, 2B,	Feces						
1C, 2C, 3C, 4C, 5C, 6C,	Tissue						
10C, 9C	Bile						

**a. Pharmacokinetic studies**

[Briefly describe how samples were handled after harvesting (shipment, storage, etc.) and any preparation that was done prior to extraction.]

[If warranted, include a graphic (i.e., flowchart) of the extraction and fractionation schemes and omit following textual description.]

[Briefly describe the extraction, fractionation and hydrolysis strategies for each tissue. The description should include solvents used (ratios), the order of their use, the extraction procedures employed (i.e., blending, maceration, Soxhlet, etc.) and procedures used to release bound and conjugated residues (i.e., acid, base, or enzyme hydrolysis, exhaustive extraction, etc.). Has the petitioner justified the use of severe conditions (e.g., strong acid hydrolysis in the presence of heat, etc.).]

**b. Metabolite characterization studies**

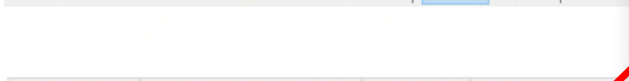
[Briefly describe the principle of the methods used for identification/characterization of the residues. Specify instrumentation (LSC, TLC, GLC, HPLC, etc.) and detection method used (UV, ECD, FID, MS/MS, etc.). State the LOD and LOQ. If applicable, very briefly describe difficulties with methods that fail to elucidate the nature of the residues or bound residues as in protein or lipid fractions.]

**3. Statistics**

[List parameters that were analyzed and the statistical methods used; include a statement that the Reviewer considers the analyses used to be appropriate. If inappropriate, provide alternative/rationale]







I. General info II. Materials and methods III. Results IV. Discussion and c

Appendix1a



Test#	Sex	Number	Dose Route	Dose (nominal)	Dose (measu
10A	Female	2	Oral	50.0 mg/kg	48.5 mg/kg
10B	Female	2	Oral	50.0 mg/kg	48.5 mg/kg
10C	Female	2	Oral	50.0 mg/kg	48.5 mg/kg

An Appendix 2 Editor window pops up, a chemical name is entered.

Appendix2 Editor

Common Name / Code

Chemical Name

Chemical Structure

Parent(s)

Expertise

None Assumed by author(s) Expertly specified

Expert

Decision

Submit Cancel

Tolerance Expression Residue of Concern

Chemical Structure

Chemical Name

Common Name / Code

Parent(s)

Expertise

None Assumed by author(s) Expertly specified

Expert

Decision

Submit Cancel

Tolerance Expression Residue of Concern

Chemical Structure

Chemical Name

Common Name / Code

Parent(s)

Expertise

None Assumed by author(s) Expertly specified

Expert

Decision

Submit Cancel

Tolerance Expression Residue of Concern

Chemical Structure

Chemical Name

Common Name / Code

Click on this icon to bring up the STRUCTURE DRAWING EDITOR – follow directions from previous section in this guidance referring to structural drawing package.

Expertise may be added to a given structure. “Assumed by Author” is reserved for a structure presented by the Author in a submitted map but for which there is no proof via detection experimentally. “Expertly specified” is used to provide a likely structure whereby the Author did not definitively draw the exact location of ring-hydroxylation or conjugation for example. The Expert may then specify such a structure with some knowledge listed to base that decision.

**We will start by adding the parent structure – as was done in the materials & methods using COPY/PASTE of the SMILES string.**

C:\Users\rkolancz\0\_Working Files\MetaPath Users Group\EFSA Contract\Mesotrione.xml - DER Composer

DER Composer v5.2 (Rat/Livestock)  
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Appendix2 Editor

Common Name / Code  
Mesotrione

Chemical Name

I. General info II. Materials and methods III. Results IV. 2D Editor

Test# Sex Number Dose Route Dose (nominal)

10A	Female	2	Oral	50.0 mg/kg
10B	Female	2	Oral	50.0 mg/kg
10C	Female	2	Oral	50.0 mg/kg
11A	Male	2	Oral	100.0 mg/kg
11B	Male	2	Oral	100.0 mg/kg
12A	Female	2	Oral	100.0 mg/kg
12B	Female	2	Oral	100.0 mg/kg

Appendix2

Tree List

ID	Common Name / Code	Chemical Name
1	Mesotrione	Mesotrione (ZA1296)

2D Editor

SMILES/InChI CS(=O)(=O)c1ccc(C(=O)C2C(=O)CCCC2=O)c(N(=O)=O)c1

000000-00-0

Templates Work Common Fragments

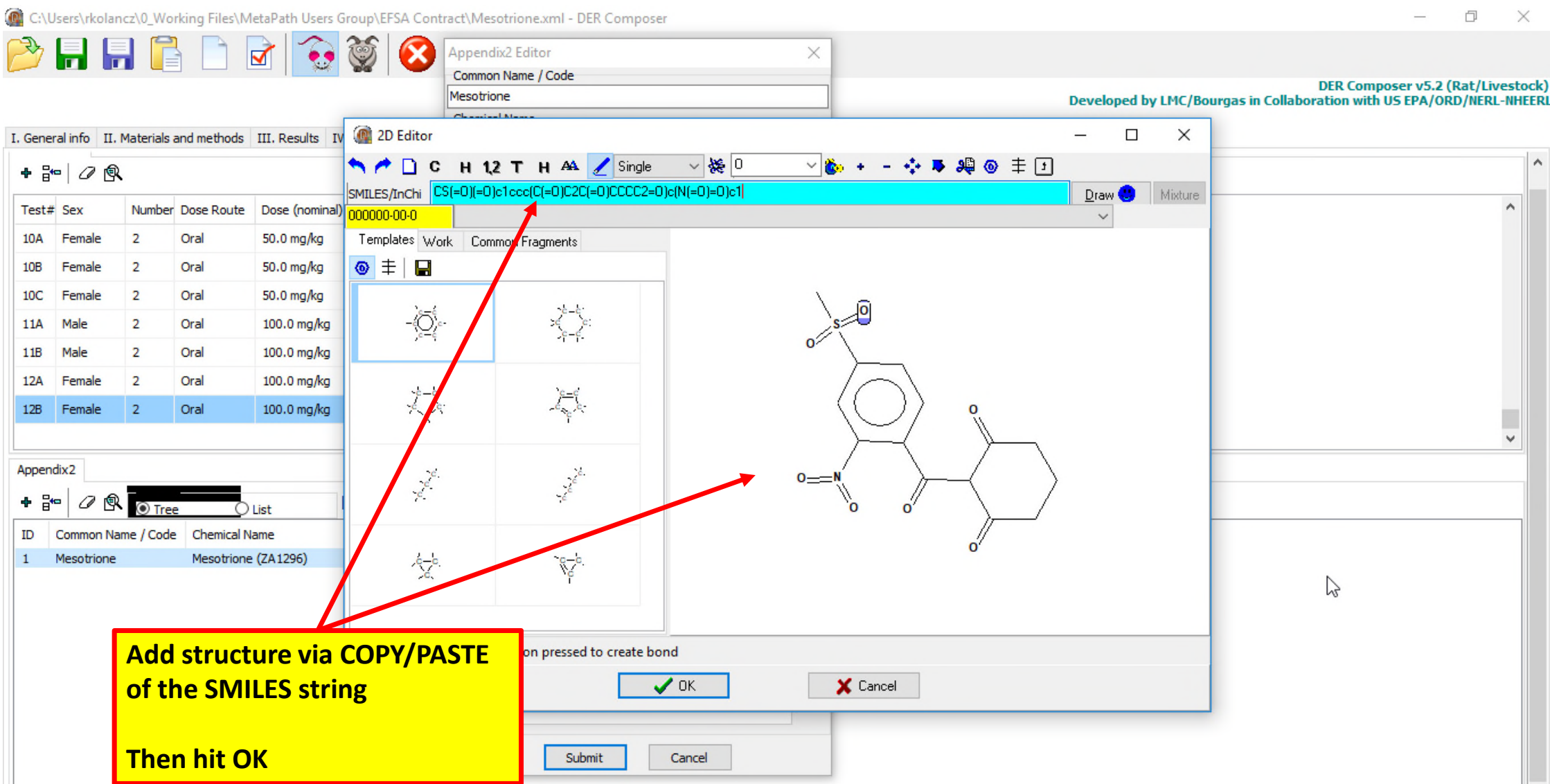
on pressed to create bond

OK Cancel

Submit Cancel

**Add structure via COPY/PASTE of the SMILES string**

**Then hit OK**





I. General info II. Materials and methods III. Results IV. Discussion and

+ -

Test#	Sex	Number	Dose Route	Dose (nominal)	Dose (measured)
10A	Female	2	Oral	50.0 mg/kg	48.5 mg/kg
10B	Female	2	Oral	50.0 mg/kg	48.5 mg/kg
10C	Female	2	Oral	50.0 mg/kg	48.5 mg/kg
11A	Male	2	Oral	100.0 mg/kg	104.8 mg/kg
11B	Male	2	Oral	100.0 mg/kg	104.8 mg/kg
12A	Female	2	Oral	100.0 mg/kg	110.7 mg/kg
12B	Female	2	Oral	100.0 mg/kg	110.7 mg/kg

Appendix2

+ - Tree List

ID	Common Name / Code	Chemical Name	SMILES
1	Mesotrione	Mesotrione (ZA1296)	

## Appendix2 Editor

Common Name / Code

Mesotrione

Chemical Name

Mesotrione (ZA1296)

Chemical Structure

CS(=O)(=O)c1ccc(C(=O)C2C(=O)CCCC2=O)c(N(=O)=O)

Parent(s)

Expertise

☒ None☐ Tolerance Expression☐ Assumed by author(s)☐ Residue of Concern☐ Expertly specified

Expert

Decision

Submit

Cancel

**SMILES string populates. Type in name. Then hit the submit button to accept structure.**

**Note: Under parent(s) section on this editor is where connectivity of the structures within the map is added. Since this structure in the example is an initial structure (parent) there is no parent which to connect.**

Modified

Rat

Test#	Sex	Number	Dose Route	Dose (nominal)	Dose (measured)	Dose Type	Test Duration	Matrix	Experimental Descriptor	Remarks
10A	Female	2	Oral	50.0 mg/kg	48.5 mg/kg	single	48 hrs	Urine		pooled samples of feces, urine, and bil
10B	Female	2	Oral	50.0 mg/kg	48.5 mg/kg	single	48 hrs	Feces		pooled samples of feces, urine, and bil
10C	Female	2	Oral	50.0 mg/kg	48.5 mg/kg	single	48 hrs	Bile		pooled samples of feces, urine, and bil
11A	Male	2	Oral	100.0 mg/kg	104.8 mg/kg	single	48 hrs	Urine		used solely as a source of fecal and ur
11B	Male	2	Oral	100.0 mg/kg	104.8 mg/kg	single	48 hrs	Feces		used solely as a source of fecal and ur
12A	Female	2	Oral	100.0 mg/kg	110.7 mg/kg	single	48 hrs	Urine		used solely as a source of fecal and ur
12B	Female	2	Oral	100.0 mg/kg	110.7 mg/kg	single	48 hrs	Feces		used solely as a source of fecal and ur

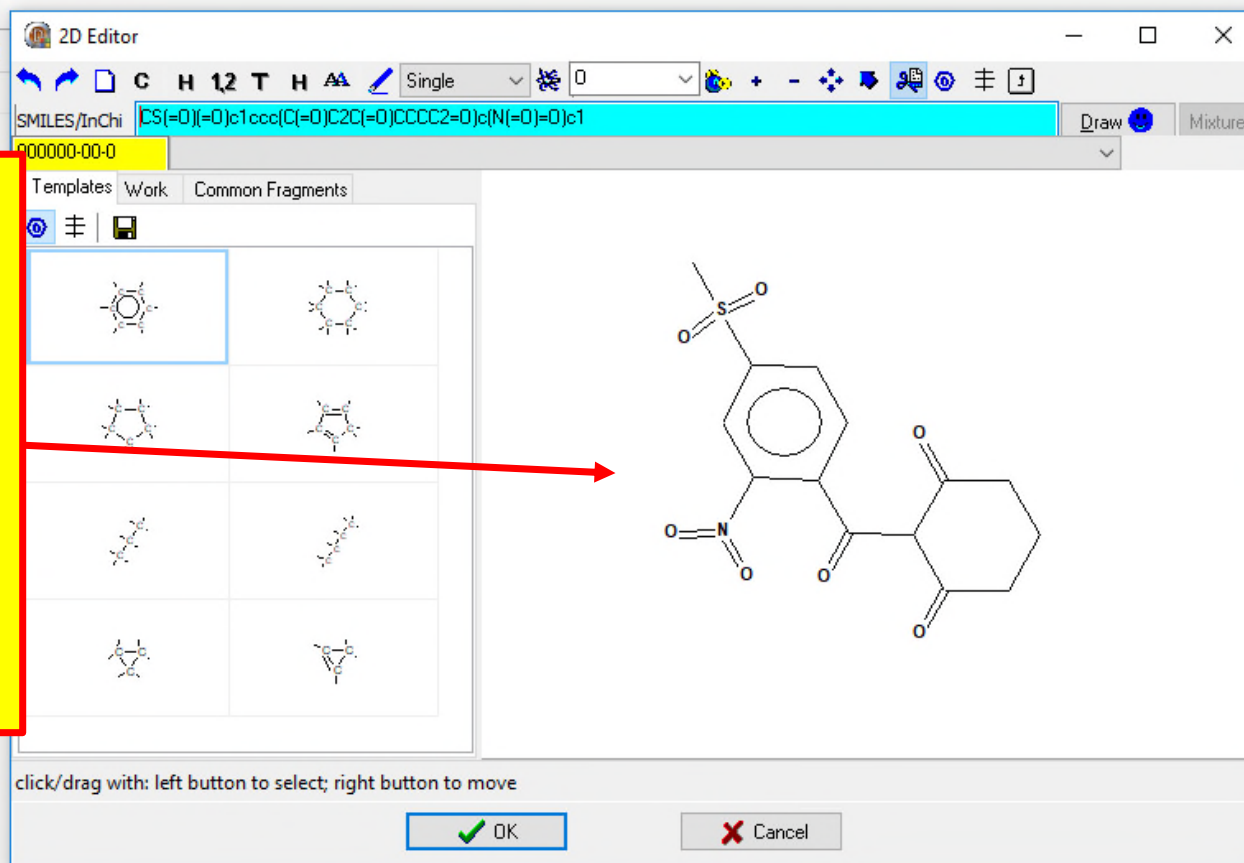
ID	Common Name / Code	Chemical Name	SMILES	Parent(s)	Expertise
1	Mesotrione	Mesotrione (ZA1296)	<chem>CS(=O)(=O)c1ccc(C(=O)C2C(=O...</chem>		

Continue with the next structure (daughter to the parent) by clicking on the + icon once again.

Click on structure drawing editor icon

DER Composer v5.2 (Rat/Livestock)  
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The parent SMILES string may be imported via COPY/PASTE to produce the parent 2-D structure and then modified to reflect the metabolite structure. With the new metabolite, usually there are only slight modifications to the parent structure. This can be a time saver rather than drawing each metabolite from scratch.



**In this example the metabolite is 5-hydroxy-mesotrione. The following steps will introduce a hydroxy group in the 5-position of the dione ring.**

C:\Users\rkolanca\0\_Working Files\MetaPath Users Group\EFSA Contract\Mesotrione.xml - DER Composer

Appendix2 Editor

Common Name / Code

Chemical Name

Chemical Structure

SMILES/InChi CC1CC(=O)C(C(=O)c2cc(S(C)(=O)O)cc2N(=O)=O)C(=O)C1

000000-00-0

2D Editor

Templates Work Common Fragments

drag the mouse with left button pressed to create bond

OK Cancel

DER Composer v5.2 (Rat/Livestock)  
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To get started, click the blue-pen icon (high-lighted as bond when the cursor is moved over the top) and move into the white box area (a little hand follows the cursor). Click on existing carbon atom and drag to give rise to a carbon – carbon bond.



To change atom type, for example from carbon to oxygen; use the periodic table option (blue circle with two yellow circles icon).

DER Composer v5.2 (Rat/Livestock)  
Developed by LMC/Bourgas in Collaboration with US EPA/ORD/NERL-NHEERL

Appendix2 Editor

Common Name / Code

Chemical Name

Chemical Structure

SMILES/InChi CC1CC(=O)C(C(=O)c2ccc(S(C)(=O)=O)cc2N(=O)=O)C(=O)C1

000000-00-0

2D Editor

Templates Work Common Fragments

Parent(s)

1 : Mesotrione (ZA1296) (CS

Expertise

☒ None

☐ Assumed by author(s)

☐ Expertly specified

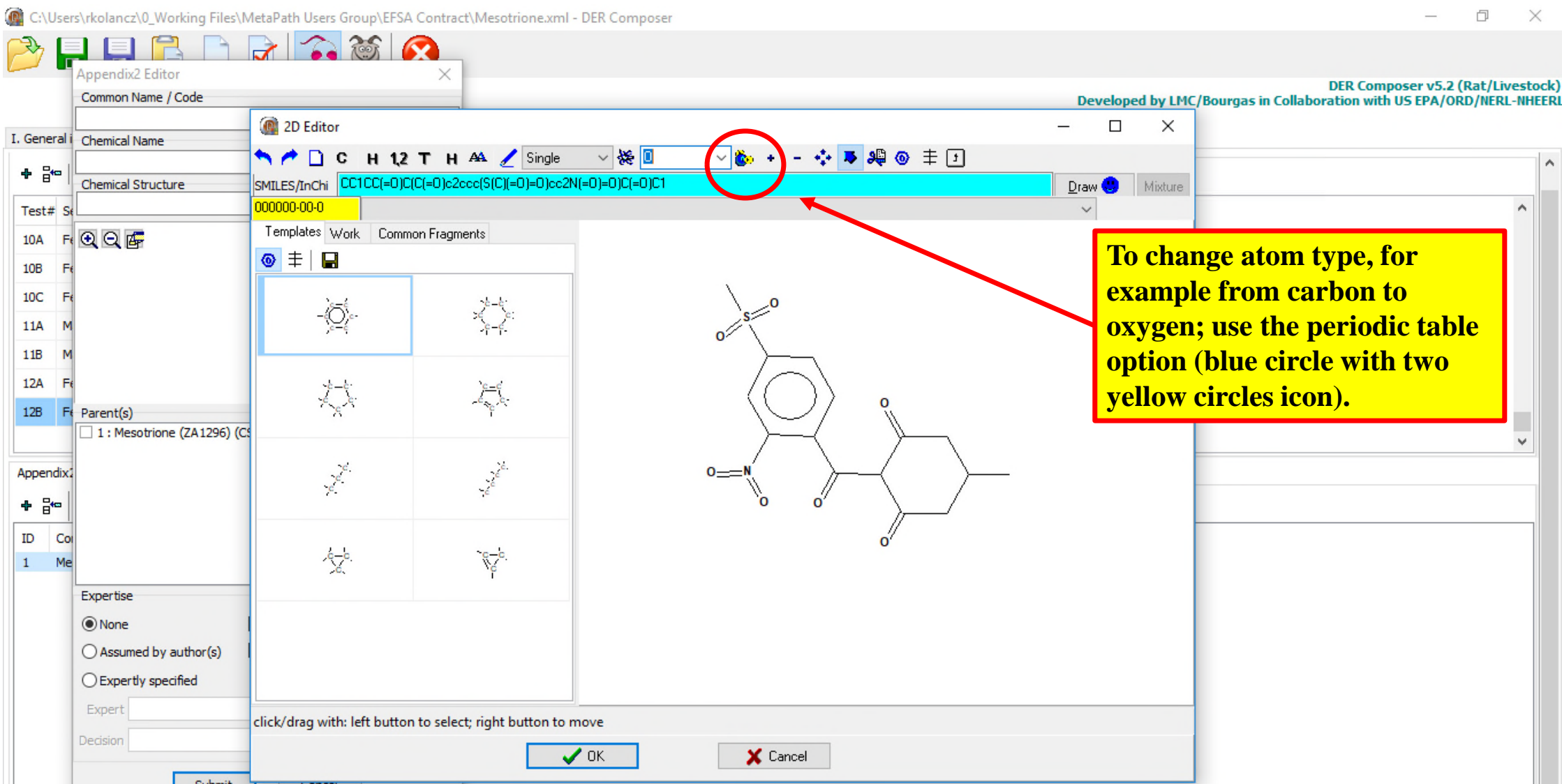
Expert

Decision

click/drag with: left button to select; right button to move

OK Cancel

To change atom type, for example from carbon to oxygen; use the periodic table option (blue circle with two yellow circles icon).



The periodic table opens, click on atom choice, click **Yes** to accept choice and the table goes away.

DER Composer v5.2 (Rat/Livestock)  
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Appendix2 Editor

Common Name / Code

Chemical Name

Chemical Structure

SMILES/InChi

000000-00-0

Templates Work

2D Editor

Periodic Table

Selected element: O

Yes Cancel Help

OK Cancel

click/drag with: left button to select; right button to move

1: Mesotrine (ZA1296) (C)

Expertise

None

Assumed by author(s)

Expertly specified

Expert

Decision

1																	2
H																	He
3	4															10	
Li	Be															Ne	
11	12															18	
Na	Mg															Ar	
19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
55	56	57	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86
Cs	Ba	*La	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
87	88	89															
Fr	Ra	*Ac															
58	59	60	61	62	63	64	65	66	67	68	69	70	71				
Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu				
90	91	92	93	94	95	96	97	98	99	100	101	102	103				
Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr				

**Simply click on the atom in the structure that you wish to replace and the substitution will be made.**

C:\Users\rkolancz\0\_Working Files\MetaPath Users Group\EFSA Contract\Mesotrione.xml - DER Composer

Appendix2 Editor

Common Name / Code

Chemical Name

Chemical Structure

SMILES/InChi CS(=O)(=O)c1ccc(C(=O)C2C(=O)CC(O)CC2=O)c(N(=O)=O)c1

000000-00-0

2D Editor

Templates Work Common Fragments

click the mouse to create/modify atom

OK Cancel

DER Composer v5.2 (Rat/Livestock)

Atom change from carbon to oxygen.

Then click OK to accept structure.

**SMILES** for metabolite is entered into **EDITOR**. Add metabolite name to **Chemical Name** and check affiliation box of parent structure for this metabolite. Hit **Submit** to accept.

C:\Users\rkolancz\0\_Working Files\MetaPath Users Group\EFSA Contract\Mesotrione.xml - DER Composer

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**Appendix2 Editor**

Common Name / Code  
5-Hydroxy-Mesotrione

Chemical Name  
5-Hydroxy-Mesotrione

Chemical Structure  
CS(=O)(=O)c1ccc(C(=O)C2C(=O)CC(O)CC2=O)c(N(=O))

Parent(s)  
☒ 1 : Mesotrione (ZA1296) (CS(=O)(=O)c1ccc(C(=O)C2C(=O)CC(O)CC2=O)c(N(=O)))

Expertise  
☒ None  
☐ Assumed by author(s)  
☐ Expertly specified  
☐ Tolerance Expression  
☐ Residue of Concern  
 Expert:   
 Decision:

Submit Cancel

Test#	Sex	Nu	Type	Test Duration	Matrix	Experimental Descriptor
10A	Female	2		48 hrs	Urine	
10B	Female	2		48 hrs	Feces	
10C	Female	2		48 hrs	Bile	
11A	Male	2		48 hrs	Urine	
11B	Male	2		48 hrs	Feces	
12A	Female	2		48 hrs	Urine	
12B	Female	2		48 hrs	Feces	

Appendix2

ID	Common Name /	Parent(s)	Expertise
1	Mesotrione		

Appendix VI. Attachments

Check box here to denote connectivity of structure 2 (5-Hydroxy-Mesotrione), the metabolite of the parent structure 1 (Mesotrione).

Then hit submit.

Note: In more complex maps the same metabolite may originate from more than one source.



**Continue filling in structures with connectivity information until the resulting table is sufficiently completed to represent the metabolic map.**

C:\Users\rkolancz\0\_Working Files\MetaPath Users Group\EFSA Contract\Mesotrione.xml - DER Composer

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**Editing button to Insert a row – highlight row for location and click and insert**

**Editing button to delete a row – highlight row for deletion and click**

**Button to edit an existing row – highlight row and click to edit – then make and accept changes**

**Option to list metabolites, degradates or residues with connectivity (Tree) or simply as a list of those found (List) within a study.**

**Completed Appendix 2 Metabolite inventory table with structure ID number, name, SMILES and connectivity.**

Test#	Sex	Number	Dose Route	Dose (nominal)	Dose (measured)	Dose	Remarks
10A	Female	2	Oral	50.0 mg/kg	48.5 mg/kg	single	ooled samples of feces, urine, and bil
10B	Female	2	Oral	50.0 mg/kg	48.5 mg/kg	single	ooled samples of feces, urine, and bil
10C	Female	2	Oral	50.0 mg/kg	48.5 mg/kg	single	ooled samples of feces, urine, and bil
11A	Male	2	Oral	100.0 mg/kg	104.8 mg/kg	single	48 hrs Urine used solely as a source of fecal and ur
11B	Male	2	Oral	100.0 mg/kg	104.8 mg/kg	single	48 hrs Feces used solely as a source of fecal and ur
12A	Female	2	Oral	100.0 mg/kg	110.7 mg/kg	single	48 hrs Urine
12B	Female	2	Oral	100.0 mg/kg	110.7 mg/kg	single	48 hrs Feces

Appendix 2

☒ Tree ☐ List

ID	Common Name / Code	Chemical Name	SMILES	Parent(s)	Expertise
1	Mesotrione	Mesotrione (ZA1296)	CS(=O)(=O)c1ccc(C(=O)C2C(=O...		
2	5-Hydroxy-Mesotri...	5-Hydroxy-Mesotrione	CS(=O)(=O)c1ccc(C(=O)C2C(=O...	1	
3	4-Hydroxy-Mesotri...	4-Hydroxy-Mesotrione	CS(=O)(=O)c1ccc(C(=O)C2C(=O...	1	
4	MNBA	MNBA	CS(=O)(=O)c1ccc(C(O)=O)c(N(=...	1	
5	Intermediate	Intermediate	CS(=O)(=O)c1ccc(C(=O)C2C(=O...	1	by Author
6	AMBA	AMBA	CS(=O)(=O)c1ccc(C(O)=O)c(N)c1	4,5	

Appendix2 Editor

Common Name / Code

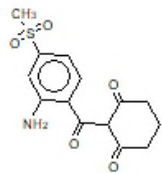
Intermediate

Chemical Name

Intermediate

Chemical Structure

CS(=O)(=O)c1ccc(C(=O)C2C(=O)CCCC2=O)c(N)c1



Parent(s)

☒ 1 : Mesotrione (ZA1296) (CS(=O)(=O)c1ccc(C(=O)C2C(=O)CCCC2=O)c(N)c1)

☐ 2 : 5-Hydroxy-Mesotrione (CS(=O)(=O)c1ccc(C(=O)C2C(=O)CCCC2=O)c(O)c1)

☐ 3 : 4-Hydroxy-Mesotrione (CS(=O)(=O)c1ccc(C(=O)C2C(=O)CCCC2=O)c(N)c1)

☐ 4 : MNBA (CS(=O)(=O)c1ccc(C(=O)C2C(=O)CCCC2=O)c(N)c1)

☐ 6 : AMBA (CS(=O)(=O)c1ccc(C(=O)C2C(=O)CCCC2=O)c(N)c1)

Expertise

☐ None ☐ Tolerance Expression

☒ Assumed by author(s) ☐ Residue of Concern

☐ Expertly specified

Expert

Decision

Submit Cancel

**Note: Structure #5 is labeled as intermediate and is listed as “Assumed By Author” under expertise which denotes that the metabolite was not found in the study but was implied by the study authors as an intermediate in the metabolic map.**

**Note: Other expertise may be entered to specify why a given structure was drawn. Example might be unspecified location for ring-hydroxylation that was drawn as a most likely position. Or perhaps a site of glucuronidation on a given structure with an explanation of why it is the most probable.**

Next go back to **II. Materials and methods** tab & sub-tab **B. Study design and methods** and fill in narrative text sections under **1. Group arrangements** and **2. Dosing and sample collection**. Tables 1a auto-populates from Appendix 1.

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I. General info

II. Materials and methods

III. Results

IV. Discussion and conclusions

V. Appendix

VI. Attachments

A. Materials

B. Study design and methods

1. Group arrangements

Animals were assigned to the test groups noted in Table1

Table 1a

Treatment Group	Sex	Number	Dose Route	Dose (nominal)	Dose (measured)	Dose Type	Remarks
6	Female	5	Oral	1.0mg/kg	1.02mg/kg	multiple	Feces,Tissue,Urine; "72 hrs"
7	Male	5	I.V.	1.0mg/kg	0.99mg/kg	single	Feces,Tissue,Urine; "72 hrs"
8	Female	5	I.V.	1.0mg/kg	1.02mg/kg	single	Feces,Tissue,Urine; "72 hrs"
9	Male	2	Oral	50.0mg/kg	49.4mg/kg	single	Bile,Feces,Urine; "48 hrs"
10	Female	2	Oral	50.0mg/kg	48.5mg/kg	single	Bile,Feces,Urine; "48 hrs"
11	Male	2	Oral	100.0mg/kg	104.8mg/kg	single	Feces,Urine; "48 hrs"
12	Female	2	Oral	100.0mg/kg	110.7mg/kg	single	Feces,Urine; "48 hrs"

2. Dosing and sample collection

Briefly describe dosing methods and sample collection

Table 2a

Treatment Group	Matrix	Sample Time	Major Method	Conjugate Analysis	Analytical Separation	Analytical Detection	Remarks
-----------------	--------	-------------	--------------	--------------------	-----------------------	----------------------	---------

Add narrative text throughout within this section.



Down further in **II. Materials and methods** tab & sub-tab **B. Study design and methods** Tables 2a auto-populates part way from Appendix 1.

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I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

A. Materials B. Study design and methods

Treatment Group	Matrix	Sample Time	Major Method	Analytical Separation	Analytical Detection	Remarks
10A, 11A, 12A, 1A, 2A	Urine					
10B, 11B, 12B, 1B, 2B,	Feces					
1C, 2C, 3C, 4C, 5C, 6C	Tissue					
10C, 9C	Bile					

**Table2 Editor**  
Matrix:  Sample Time:   
Sample Process Major Method:  Sample Process Conjugate Analysis:   
Analytical Separation:  Analytical Detection:   
Remarks:

#### a. Pharmacokinetic studies

[Briefly describe how samples were handled after harvesting (shipment, storage, etc.) and any preparation that was done prior to extraction.]

[If warranted, include a graphic (i.e., flowchart) of the extraction and fractionation schemes and omit following textual description.]

[Briefly describe the extraction, fractionation and hydrolysis strategies for each tissue. The description should include solvents used (ratios), the order of their use, the extraction procedures employed (i.e., blending, maceration, Soxhlet, etc.) and procedures used to release bound and conjugated residues (i.e., acid, base, or enzyme hydrolysis, exhaustive extraction, etc.). Has the petitioner justified the use of severe conditions (e.g., strong acid hydrolysis in

#### b. Metabolite characterization studies

[Briefly describe the principle of the methods used for identification/characterization of the residues. Specify instrumentation (LSC, TLC, GLC, HPLC, etc.) and detection method used (UV, ECD, FID, MS/MS, etc.). State the LOD and LOQ. If applicable, very briefly describe how bound residues as in protein or lipid fractions.]

To finish filling out information in Table 2a, move cursor to line in table to be edited and click this EDIT button. The blue-box Table 2 EDITOR will come up.

Make edits and click Submit.

Finnish adding text

Modified

Rat

2:50 PM  
2/17/2021

# Go To Live Demo

C:\Users\rkolanca\Documents\UnnamedDER.xml - DER Composer

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I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

Appendix1

+ [icon] [icon] [icon]

Test#	Sex	Number	Dose Route	Dose (nominal)	Dose (measured)	Dose Type	Test Duration	Matrix	Experimental Descriptor	Remarks

Appendix2

+ [icon] [icon] [icon] [icon] [icon] [icon]

Tree List

ID	Common Name / Code	Chemical Name	SMILES	Parent(s)	Expertise

Rat

11:23 AM 4/13/2021

Questions ???  
&  
Answers



# Part 3:

- **Results**

**(Pharmacokinetic studies)**

**III. Results tab & sub-tab A. Pharmacokinetic studies.** There are sub-tabs for preliminary experiment, Absorption, Other, Excretion, and Half-life. Each will display a sample table and table construction will essentially follow the same process for each tab. Below are functions of button bar icons.

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I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

A. Pharmacokinetic studies B. Metabolite characterization studies

Preliminary experiment Absorption Other Excretion Halflife

(if applicable)(Briefly describe results)

Sample Table

Icon – To Hide or Show Sample Table

Icon – To Copy a Whole Table

Icon – To Paste a Whole Table

Icon – Manage Columns

Icon – Delete a Row

Icon – Insert a Row

Icon – Add a Row

Icon - Delete Table

Icon – Add Table

Table Title

Columns Title

Rat

I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

A. Pharmacokinetic studies B. Metabolite characterization studies

Preliminary experiment Absorption Other Excretion Halflife

(include treatment groups that are applicable)(describe excretion patterns for each treatment group)

Click on the Icon to Add Table Under Excretion Tab



Table6a

Table Title Recovery over time of radioactivity in excreta of rats following a single

Add Title for Table

Columns Title Percent of radioactive dose administered

Add a Column Title – Example “Percent of Administered Dose”

Modified Rat

I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

A. Pharmacokinetic studies B. Metabolite characterization studies

Preliminary experiment Absorption Other Excretion Half-life

(include treatment groups that are applicable)(describe excretion patterns for each treatment group)

Click on Manage Column Icon – Brings up Editor Box



Table6a

Table Title Recovery over time of radioactivity in excreta of rats following a single

Columns Title Percent of radioactive dose administered

Tissue/Excre

Columns Editor

Test	Matrix	Column	General Label
		6 hr	male

Custom Column  
12 hr Add

General Column Label:  
male Set

Close

Add General Column Label Ex/ "male" by Clicking on Custom Column Above and then Set to Affix Label

Add Custom Column Ex/ "12 hr" and Click Add

Continue by Adding Custom Columns & Labels Until the Time Points 6, 12, 24, 36, 48, 72 hrs and Total are Created for Both Males and Females

Modified

Rat

**Completed Addition of Custom Columns & Labels  
for the Time Points 6, 12, 24, 36, 48, 72 hrs and  
Total for Both Males and Females**

**Click Close When Done with Editor**

I. General info II. Materials and methods III. Results IV. Discussion and

A. Pharmacokinetic studies B. Metabolite characterization studies

Preliminary experiment Absorption Other Excretion Halflife

(include treatment groups that are applicable)(describe excretion patterns for each treatment group)

Table6

Table6a

Table Title Recovery over time of radioactivity in excreta of rats following a single

Columns Title Percent of radioactive dose administered

Tissue/Excretion

**Columns Editor**

Test	Matrix
24 hr	female
36 hr	female
48 hr	female
72 hr	female
Total	female

Custom Column:  Add

General Column Label:  Set

Close

Modified

Rat

9:49 AM  
3/22/2021

I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

A. Pharmacokinetic studies B. Metabolite characterization studies

Preliminary experiment Absorption Other Excretion Half-life

(include treatment groups that are applicable)(describe excretion patterns for each treatment group. Some form of table 3 is recommended)

Table6

Table6a

Table Title Recovery over time of radioactivity in excreta of rats following a single

Columns Title Percent of radioactive dose administered

	male	male	male	male	male	male	male	female	female	female	female	female	female	female
Tissue/Excre	6 hr	12 hr	24 hr	36 hr	48 hr	72 hr	Total	6 hr	12 hr	24 hr	36 hr	48 hr	72 hr	Total

Add Rows to Table

Modified

Rat



## I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

## A. Pharmacokinetic studies B. Metabolite characterization studies

## Preliminary experiment Absorption Other Excretion Halflife

(include treatment groups that are applicable)(describe excretion patterns for each treatment group. Some form of table 3 is recommended)

Table6

Table6a

Table Title Recovery over time of radioactivity in excreta of rats following a single

Columns Title Percent of radioactive dose administered

Enter a single numerical entry or "+"

	male	male	male	male	male	male	male	female	female	female	female	female	female	female
Tissue/Excreta	6 hr	12 hr	24 hr	36 hr	48 hr	72 hr	Total	6 hr	12 hr	24 hr	36 hr	48 hr	72 hr	Total
Urine	44.02	7.16	1.77	0.51	0.33	0.36	54.15	44.49	5.63	3.05	0.97	0.84	0.90	55.88
Feces		12.12	9.23	1.94	0.72	0.50	24.50		8.92	11.29	2.15	0.82	0.62	23.80
Total	44.02	19.28	11.00	2.45	1.05	0.86	78.65	44.49	14.55	14.34	3.12	1.66	1.52	79.63

**Population of Values to  
Complete the Table****Rows Added to Table**

Modified

Rat

## I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

## A. Pharmacokinetic studies B. Metabolite characterization studies

## Preliminary experiment Absorption Other Excretion Halflife

Absorption and excretion - Following a single oral dose of [14C-aromatic]mesotrione at 5.0 mg/kg, excretion in the urine for the males was rapid with 54.1-58.6% of the dose being excreted in the urine within 6 hours of dosing (Table 2), equivalent to 75-88% of the total urinary excretion. In the single male kept to 48 hours, overall excretion in urine and feces, was essentially complete within 24 hours and accounted for 90.2% of the dose, equivalent to 97% of the total excretion. Following oral dosing of (14C- aromatic)mesotrione at 5.0 mg/kg, excretion in the urine for the females was slower than the males with only 19.3-20.9% of the dose being excreted in the urine within 6 hours of dosing, equivalent to 39-46% of the total urinary excretion. In the single female kept to 48 hours, overall excretion in urine and feces, was essentially complete within 24 hours and accounted for 48.1% of the dose, equivalent to 64% of the total excretion. Recovery of total radioactivity was lower in females when compared to males with only 52.9-75.6% of the total administered dose recovered for the females vs 92.8-100.9% of the dose recovered for the males. Less than 0.1% of the dose was recovered from exhaled air in both sexes.

Table6

Table6a Table6b Table6c Table6d

Table Title Recovery over time of radioactivity in excreta of rats following a single

Columns Title Percent of radioactive dose administered

	male	male	male	male	male	male	male	female	female	female	female	female	female	female
Tissue/Excreta	6 hr	12 hr	24 hr	36 hr	48 hr	72 hr	Total	6 hr	12 hr	24 hr	36 hr	48 hr	72 hr	Total
Urine	70.68	5.85	1.65	0.62	0.40	0.19	79.39	75.06	4.75	2.15	1.14	0.59	0.45	84.14
Feces		2.61	3.05	0.59	0.28	0.24	6.77		0.71	1.08	0.21	0.19	0.16	2.35
Total	70.68	8.46	4.70	1.21	0.68	0.43	86.16	75.06	5.46	3.23	1.35	0.78	0.61	86.49

Population of Text

Addition of Multiple Tables

# Go To Live Demo

C:\Users\rkolancz\Documents\UnnamedDER.xml - DER Composer

DER Composer v5.2 (Rat/Livestock)  
Developed by LMC/Bourgais in Collaboration with US EPA/ORD/NERL-NHEERL

I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

A. Pharmacokinetic studies B. Metabolite characterization studies

Preliminary experiment Absorption Other Excretion Halflife

(include treatment groups that are applicable)(describe excretion patterns for each treatment group. Some form of table 3 is recommended)

Table6

Table Title [Type Title Here]

Columns Title Percent of administered dose

Rat

11:23 AM 4/13/2021

Questions ???  
&  
Answers

# Part 4:

- **Results**

**(Metabolite characterization studies)**

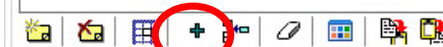


## I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

## A. Pharmacokinetic studies B. Metabolite characterization studies

aromatic] mesotrione either iv at a target dose of 1.00 mg/kg or orally (gavage) at target doses of 1.00 or 100 mg/kg or 1.00 mg/kg following a 14-day pretreatment with nonlabeled mesotrione at 1.00 mg/kg/day. A group composed for bile-duct cannulated rats (2/sex) were also dosed once orally with [14C-aromatic]mesotrione at 50 mg/kg to examine biliary excretion. To assess the effect of 14C-label position within the molecule on metabolism and excretion, a final group of bile-duct cannulated rats (2/sex) was dosed once orally with [14C-dione]mesotrione at a target dose of 50 mg/kg.

Animals were randomly assigned to dose groups. Actual average doses for each test group are presented in Table 1 and were within 96-102% of the nominal 1.00 mg/kg dose, 94-99% of the nominal 50.0 mg/kg dose, and 99-111 % of the nominal 100 mg/kg dose.



**Also is Critical to Use the Treatment Groups as Described in Appendix 1. We Need to Conserve the Relationship Between Treatment Group and Metabolite in the Interest of Maintaining the Highlight Treatment Group Function. Click on this Icon for Access to a Listing of Potential Columns when Constructing the Table(s).**

Table8a  
Table Title  
Columns Title

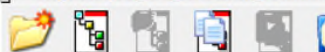
Compound
Mesotrione
5-Hydroxy-Mesotrione
4-Hydroxy-Mesotrione
MNBA
Intermediate
AMBA

**Under Metabolite Characterization Tab – When a New Table is Added a List of Metabolites (From Appendix 2) Are Automatically Populated. This is Important as These Exact Names are Critical for the Eventual Import into MetaPath Regarding the “Highlight Treatment Group” Function.**



Developed by LMC Bourgas in collaboration with US EPA / ORD / NERL-NHEERL

RegulatoryDB\_771\_June 2020\_v3.3.0.MTB



Locked by: administrator

Regulatory ID quick search

ID   
Value

- 1. 220899-03-6; Metrafenone [B]
- 2. 220899-03-6; Metrafenone [T]
- 3. 149877-41-8; Bifenazate [14C]
- 4. 28057-48-9; d-Trans-Allethrin
- 5. 28057-48-9; d-Trans-Allethrin
- 6. 150114-71-9; Aminopyralid [pe]
- 7. 57960-19-7; Acequinocyl [dod]
- 8. 57960-19-7; Acequinocyl [phe]
- 9. 741-58-2; Bensulide [phenyl rir]
- 10. 335104-84-2; Tembotrione [1]
- 11. 335104-84-2; Tembotrione [1]
- 12. 420-04-2; Cyanamide [C14]
- 13. 8018-01-7; Mancozeb [14C-e]
- 14. 239110-15-7; Flupicolid [14]
- 15. 239110-15-7; Flupicolid [ph]
- 16. 272451-65-7; Flubendiamide
- 17. 272451-65-7; Flubendiamide
- 18. 272451-65-7; Flubendiamide

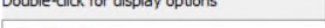
IUPAC name Metrafenone; (3-bromo-6-me

Name Metrafenone [Bromophenyl-6

CAS 220899-03-6

SMILES Cc1cc(OC)c(OC)c(OC)c1C(=C

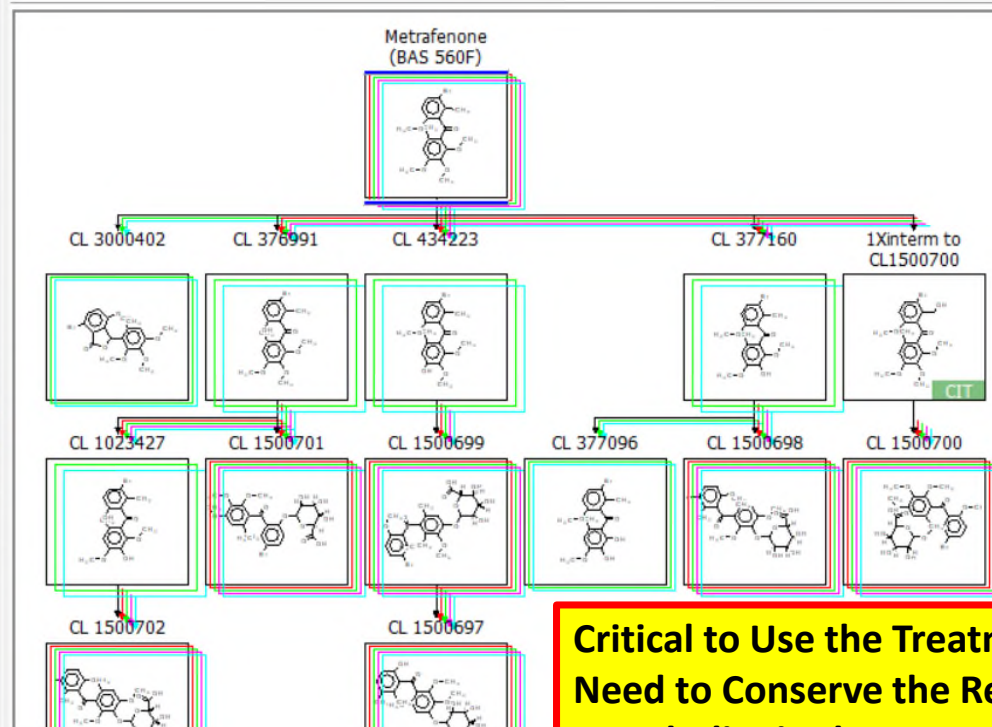
Double-click for display options



Tree Results, met. Results, PK



CAS:220899-03-6; Metrafenone [Bromophenyl-6-14C] (BAS 560F)  
Rat, in vivo (x8)



Metabolic Pathways - Highlight treatment groups

Common fields:

Rat; in vivo; oral; 10 mg/kg; nominal measured dose; radiolabeled parent; single dose; Sprague-Dawley (CrI:CD BR); single oral low dose; 168 h

Coloring and specifics:

- ☒ [1a] male; urine
- ☒ [1b] male; feces
- ☒ [1c] male; cage wash
- ☒ [1d] male; tissues
- ☒ [2a] female; urine
- ☒ [2b] female; feces
- ☒ [2c] female; cage wash

Treatment group:

Rat, Female, in vivo, feces, oral, 10 mg/kg, single dose (radiolabeled), Sprague-Dawley (CrI:CD BR), 168 h

Citations:

Mallipudi, N.M. (2002) BAS 560F (AC 375839): absorption, distribution, metabolism, and excretion study in the rat. BASF Corporation, BASF Agro Research, Princeton, NJ, and Xenobiotic Laboratories, Inc., Plainsboro, NJ. Laboratory Project Identification: 98025, April 30, 2002. MRID 46415747. Unpublished.

Subjects:

- Species - Rat
- Gender - Female (5 subjects)
- Weight - Between 150 - 350 grams (female)
- Age - Between 6 - 10 weeks old
- Strain - Sprague-Dawley (CrI:CD BR)
- Source - Charles River Laboratories (Kingston, NY) for normal animals; Hilltop Lab Animals (Scottsdale, PA) for bile-duct cannulated animals
- Housing - For the preliminary excretion study, rats were housed individually in glass metabolism cages. For all other studies, rats were housed individually in stainless steel metabolism cages
- Diet - Lab Diet 5002 certified rodent diet (PMI Nutrition, St. Louis, MO), ad libitum
- Water - Tap water, ad libitum

Environmental conditions:

- Env. temperature - Between 16 - 24 °C
- Humidity - Between 30 - 70 %
- Air changes - Not provided
- Photoperiod - 12 h light/12 h dark

In vivo / in vitro:

- In vivo
- Exper. descriptors (general) - single oral low dose

Critical to Use the Treatment Groups as Described in Appendix 1. We Need to Conserve the Relationship Between Treatment Group and Metabolite in the Interest of Maintaining the Highlight Treatment Group Function in MetaPath.

There is a List of Entered Tests (Directly from Appendix 1) Shown in the Left Panel. To Add Those Tests as Columns in the Table, Highlight and Click on the “+” Icon. To Remove an Errantly Added Test, Highlight and Click on the Eraser Icon. General Custom Labels Can Be Added Ex/ “Male-Low-Urine”, using the Feature in the Lower Right Box.

DER Composer v5.2 (Rat/Livestock)  
Collaboration with US EPA/ORD/NERL-NHEERL

I. General info II. Materials and method

A. Pharmacokinetic studies B. Metabolism

aromatic] mesotrione either iv at a target dose of 50 mg/kg or orally at a target dose of 50 mg/kg. The animals were also dosed once orally with [14C-aromatic] mesotrione at 50 mg/kg to examine biliary excretion. To assess the effect of the 14C-label position within the molecule on metabolism and excretion, a final group of bile-duct cannulated rats (2/sex) was dosed once orally with [14C-dione] mesotrione at a target dose of 50 mg/kg.

Animals were randomly assigned to dose groups. Actual average doses for each test group are presented in Table 1 and were within 96-102% of the nominal 100 mg/kg dose, 94-99% of the nominal 50.0 mg/kg dose, and 99-111 % of the nominal 100 mg/kg dose.

Table8

Table8a

Table Title wing oral dosing with [14C-aromatic] mesotrione at 1.00 or 100 mg/kg

Columns Title Percent of administered dose

Compound
Mesotrione
5-Hydroxy-Mesotrione
4-Hydroxy-Mesotrione
MNBA
Intermediate
AMBA

Columns Editor

Test	Matrix
3A	Urine
3B	Feces
3C	Tissue
4A	Urine
4B	Feces

Columns

Column	General Label
2B	Female-Low-Fe..
3A	Male-High-Urine
3B	Male-High-Feces
4A	Female-High-Ur..
4B	Female-High-F...

Custom Column

General Column Label

Female-High-Feces

Set

Close

Modified Rat

7:39 AM 3/23/2021



## I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix

## A. Pharmacokinetic studies B. Metabolite characterization studies

**Add Table Title**

aromatic] mesotrione either iv at a target dose of 1.00 mg/kg or orally (gavage) at target doses of 1.00 or 100 mg/kg or 1.00 mg/kg following a 14-day pretreatment with nonlabeled mesotrione at 1.00 mg/kg/day. A group composed for bile-duct cannulated rats (2/sex) were also dosed once orally with [14C-aromatic]mesotrione at 50 mg/kg to examine biliary excretion. To assess the effect of 14C-label position within the molecule on metabolism and excretion, a final group of bile-duct cannulated rats (2/sex) was dosed once orally with [14C-dione]mesotrione at a target dose of 50 mg/kg.

Animals were randomly assigned to dose groups. Actual average doses for each test group are presented in Table 1 and Table 2. The average dose for the 1.00 mg/kg dose, 94-99% of the nominal 50.0 mg/kg dose, and 99-111 % of the nominal 100 mg/kg dose.

**Add Column Title**

Table8

Table8a

Table Title wing oral dosing with [14C-aromatic] mesotrione at 1.00 or 100 mg/kg.

Enter a single numerical entry or "+"

Columns Title Percent of administered dose

	Male-Low-Urine	Male-Low-Feces	Female-Low-Urine	Female-Low-Feces	Male-High-Urine	Male-High-Feces	Female-High-Urine	Female-High-Feces
Compound	1A	1B	2A	2B	3A	3B	4A	4B
Mesotrione								
5-Hydroxy-Mesotrione								
4-Hydroxy-Mesotrione								
MNBA								
Intermediate								
AMBA								

**Columns Resulting from the Editor. Basic Structure of Table.**

Modified

Rat

## I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

## A. Pharmacokinetic studies B. Metabolite characterization studies

aromatic] mesotrione either iv at a target dose of 1.00 mg/kg or orally (gavage) at target doses of 1.00 or 100 mg/kg or 1.00 mg/kg following a 14-day pretreatment with nonlabeled mesotrione at 1.00 mg/kg/day. A group composed for bile-duct cannulated rats (2/sex) were also dosed once orally with [14C-aromatic]mesotrione at 50 mg/kg to examine biliary excretion. To assess the effect of 14C-label position within the molecule on metabolism and excretion, a final group of bile-duct cannulated rats (2/sex) was dosed once orally with [14C-dione]mesotrione at a target dose of 50 mg/kg.

Animals were randomly assigned to dose groups. Actual average doses for each test group are presented in Table 1 and were within 96-102% of the nominal 1.00 mg/kg dose, 94-99% of the nominal 50.0 mg/kg dose, and 99-111 % of the nominal 100 mg/kg dose.

Table8

Table8a

Table Title wing oral dosing with [14C-aromatic] mesotrione at 1.00 or 100 mg/kg.

Columns Title Percent of administered dose

Enter a single numerical entry or "+"

	Male-Low-Urine	Male-Low-Feces	Female-Low-Urine	Female-Low-Feces	Male-High-Urine	Male-High-Feces	Female-High-Urine	Female-High-Feces
Compound	1A	1B	2A	2B	3A	3B	4A	4B
Mesotrione	47	3	53	7	56	8	59	3
5-Hydroxy-Mesotrione		2				2		2
4-Hydroxy-Mesotrione	5	1			3			
MNBA		1	1	2	1	2	1	1
Intermediate								
AMBA	1	2		5		5		12

Wherever a Value (Numerical) is Placed within a Cell, it Indicates an Established Correspondence Between Treatment Group and Metabolite. This will then Pass into MetaPath upon Import defining the "Highlight Treatment Group" Function.

If a Metabolite is NOT found in a Treatment Group, Leave the Cell Blank. DO NOT Populate with a N.D. or "-".

Modified

Rat



## I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

## A. Pharmacokinetic studies B. Metabolite characterization studies

aromatic] mesotrione either iv at a target dose of 1.00 mg/kg or orally (gavage) at target doses of 1.00 or 100 mg/kg or 1.00 mg/kg following a 14-day pretreatment with nonlabeled mesotrione at 1.00 mg/kg/day. A group composed for bile-duct cannulated rats (2/sex) were also dosed once orally with [14C-aromatic]mesotrione at 50 mg/kg to examine biliary excretion. To assess the effect of 14C-label position within the molecule on metabolism and excretion, a final group of bile-duct cannulated rats (2/sex) was dosed once orally with [14C-dione]mesotrione at a target dose of 50 mg/kg.

Animals were randomly assigned to dose groups. Actual average doses for each test group are presented 94-99% of the nominal 50.0 mg/kg dose, and 99-111 % of the nominal 100 mg/kg dose.

Use These Icons to Add or Insert a New Row



Table8a

Table Title 1.00 or 100 mg/kg.

Columns Title Percent of administered dose

	Male-Low-Urine	Male-Low-Feces	Female-Low-Urine	Female-Low-Feces	Male-High-Urine	Male-High-Feces	Female-High-Urine	Female-High-Feces
Compound	1A	1B	2A	2B	3A	3B	4A	4B
5-Hydroxy-Mesotrione		2				2		2
4-Hydroxy-Mesotrione	5	1						
MNBA		1	1	2				1
Intermediate								
AMBA	1	2		5				12
Unidentified Metabolites								
Tissues								
Cage Wash								
Total Accounted For								

To Finish the Table, Additional Rows can be Added to Describe for Ex/ "Unidentified Metabolites", "Tissues", "Cage Wash", and "Total Accounted For", etc....

# Go To Live Demo

C:\Users\ykolancz\Documents\UnnamedDER.xml - DER Composer

DER Composer v5.2 (Rat/Livestock)  
Developed by LMC/Bourgas in Collaboration with US EPA/ORD/NIERL-NHEERL

I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

A. Pharmacokinetic studies B. Metabolite characterization studies

[Describe the methods used to conduct the metabolism study and to analyze the residues. Discuss any impact that the methods per se may have had on the results. Discuss the method's ability to extract the predominant residues from the various livestock matrices. Report the accountability. Has the petitioner demonstrated that residues are stable during storage?]

[Describe the residues in terms of levels, location in the livestock matrices (i.e., partitioning into fat vs. muscle vs. milk, etc.). Point out the predominant residues. Note that this is a stand-alone evaluation of the metabolism study. As such, it is not appropriate to discuss residues of concern in this document.]

[Include the amount (%TRR and ppm) of parent and/or metabolites identified in the extracted and non-extracted fractions of each commodity/matrix. Create two table templates: (1) Distribution of residues and (2) Summary of characterization and identification, see example. When available, include summary of

Table8

Table Title	[Type Title Here]
Columns Title	Percent of administered dose

Rat

11:28 AM  
4/13/2021

Questions ???  
&  
Answers

# Part 5:

- **Conclusions**
- **XML**
- **.DOC File Generation of Report**

I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

A. Pharmacokinetic studies B. Metabolite characterization studies

B. Study Design - These studies were designed to determine the absorption, metabolism, distribution, and excretion of [14C]mesotrione in rats as a function of single or repeated oral dosing, or a single intravenous dose. A preliminary study consisted of two groups of Alpk:APISD rats (2/sex/dose group) that were dosed once with [14C-aromatic]mesotrione or [14C-dione]mesotrione at a target dose of 5 mg/kg. The main mass balance study consisted of four groups of Alpk:APISD rats (5/sex/dose group) that were dosed once with [14C-aromatic] mesotrione either iv at a target dose of 1.00 mg/kg or orally (gavage) at target doses of 1.00 or 100 mg/kg. A group of bile-duct cannulated rats (2/sex) were also dosed once orally with [14C-aromatic]mesotrione at 50 mg/kg to examine biliary excretion. To assess the excretion of [14C-dione]mesotrione, a final group of bile-duct cannulated rats (2/sex) was dosed once orally with [14C-dione]mesotrione at a target dose of 50 mg/kg.

**Save or Save As the XML****Might be a good idea to do frequent saves of your work during the data capture process.**

Table8

Table8a

Table Title 1.00 or 100 mg/kg.

Columns Title Percent of administered dose

Enter a single

	Male-Low-Urine	Male-Low-Feces	Female-Low-Urine	Female-Low-Feces	Male-High-Urine	Male-High-Feces	Female-High-Urine	Female-High-Feces
Compound	1A	1B	2A	2B	3A	3B	4A	4B
5-Hydroxy-Mesotrione		2				2		2
4-Hydroxy-Mesotrione	5	1			3			
MNBA		1	1	2	1	2	1	1
Intermediate								
AMBA	1	2		5		5		12
Unidentified Metabolites	12	8	11	1	6	4	5	5
Tissues	7		6		9		3	
Cage Wash	7		12		5		8	
Total Accounted For	79	17	83	15	80	21	76	23

Modified

Rat



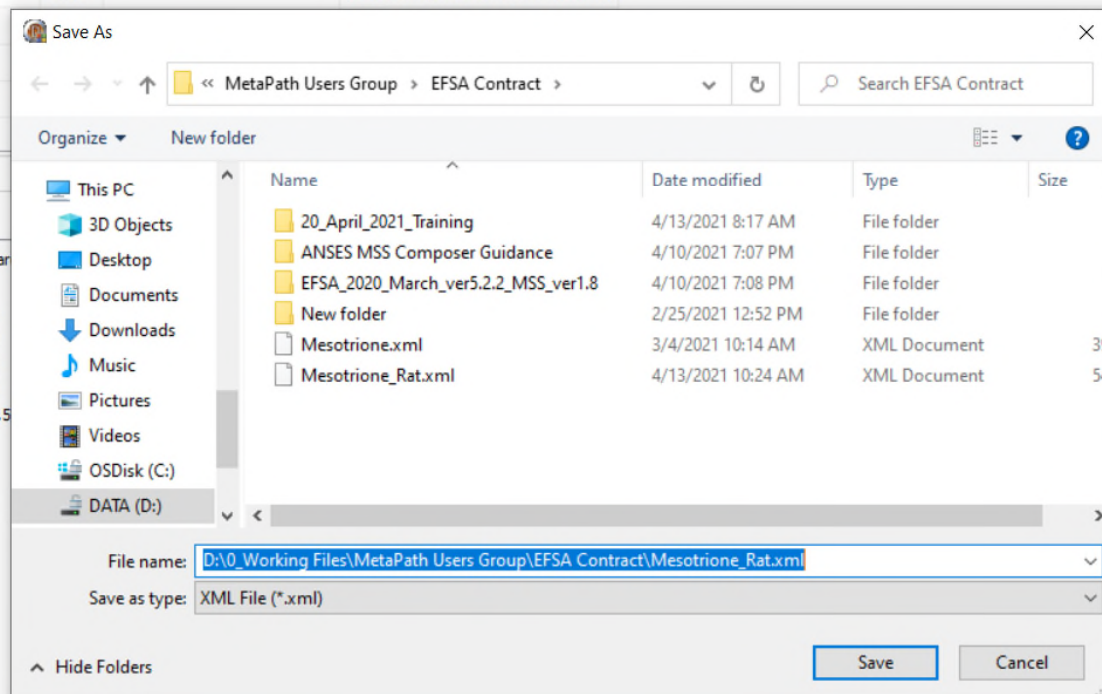
## I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

## Appendix 1a

Test#	Sex	Number	Dose Route	Dose (nominal)	Dose (measured)	Dose Type	Test Duration	Matrix	Experimental Descriptor	Remarks
1A	Male	5	Oral	100 mg/kg	100.11 mg/kg	single	72 hrs	Urine		pooled samples of urine and feces from
1B	Male	5	Oral	100 mg/kg	100.11 mg/kg	single	72 hrs	Feces		pooled samples of urine and feces from
1C	Male	5	Oral	100 mg/kg	100.11 mg/kg	single	72 hrs	Tissue		pooled samples of urine and feces from
2A	Female	5	Oral	100 mg/kg	98.79 mg/kg	single	72 hrs	Urine		pooled samples of urine and feces from
2B	Female	5	Oral	100 mg/kg	98.79 mg/kg	single	72 hrs			
2C	Female	5	Oral	100 mg/kg	98.79 mg/kg	single	72 hrs			
3A	Male	5	Oral	1.0 mg/kg	1.0 mg/kg	single	72 hrs			
3B	Male	5	Oral	1.0 mg/kg	1.0 mg/kg	single	72 hrs			

## Appendix 2

ID	Common Name / Code	Chemical Name	SMILES	Par
1	Mesotrione	Mesotrione (ZA1296)	CS(=O)(=O)c1ccc(C(=O)C2C(=O)...	
2	5-Hydroxy-Mesotri...	5-Hydroxy-Mesotrione	CS(=O)(=O)c1ccc(C(=O)C2C(=O)...	1
3	4-Hydroxy-Mesotri...	4-Hydroxy-Mesotrione	CS(=O)(=O)c1ccc(C(=O)C2C(=O)...	1
4	MNBA	MNBA	CS(=O)(=O)c1ccc(C(=O)C2C(=O)...	1
5	Intermediate	Intermediate	CS(=O)(=O)c1ccc(C(=O)C2C(=O)...	1
6	AMBA	AMBA	CS(=O)(=O)c1ccc(C(=O)C2C(=O)...	4,5



Rat



I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

A. Pharmacokinetic studies B. Metabolite characterization studies

B. Study Design - These studies were designed to determine the absorption, metabolism, distribution, and excretion of [14C]mesotrione in rats as a function of single or repeated oral dosing, or a single intravenous dose. A preliminary study consisted of two groups of Alpk:APISD rats (2/sex/dose group) that were dosed once with [14C-aromatic]mesotrione or [14C-dione]mesotrione at a target dose of 5 mg/kg. The main mass balance study consisted of four groups of Alpk:APISD rats (5/sex/dose group) that were dosed once with [14C-aromatic] mesotrione either iv at a target dose of 1.00 mg/kg, or orally (gavage) at target doses of 1.00 or 100 mg/kg. A group composed for bile-duct cannulated rats (2/sex) were also dosed once orally with [14C-aromatic]mesotrione at 50 mg/kg to examine biliary excretion. To assess the excretion of [14C-dione]mesotrione at a target dose of 50 mg/kg, a final group of bile-duct cannulated rats (2/sex) was dosed once orally with [14C-dione]mesotrione at a target dose of 50 mg/kg.

**Generate the WORD Document.****The WORD Document can then  
be Modified as you would any  
WORD Document to Conform to  
Report Style and Content.**

Table8

Table8a

Table Title 1.00 or 100 mg/kg.

Columns Title Percent of administered dose

Enter a single

	Male-Low-Urine	Male-Low-Feces	Female-Low-Urine	Female-Low-Feces	Male-High-Urine	Male-High-Feces	Female-High-Urine	Female-High-Feces
Compound	1A	1B	2A	2B	3A	3B	4A	4B
5-Hydroxy-Mesotrione		2				2		2
4-Hydroxy-Mesotrione	5	1			3			
MNBA		1	1	2	1	2	1	1
Intermediate								
AMBA	1	2		5		5		12
Unidentified Metabolites	12	8	11	1	6	4	5	5
Tissues	7		6		9		3	
Cage Wash	7		12		5		8	
Total Accounted For	79	17	83	15	80	21	76	23

Modified

Rat

## DATA EVALUATION RECORD

**STUDY TYPE:** Metabolism rat; OPPTS 870.7485[85-1]; OECD 417

**AGENCY CODE(S):** (CAS NUMBER) 104206-82-8, (US EPA PC CODE) 122990

**DP BARCODE:**  
**SUBMISSION NO.:**

**TEST MATERIAL COMMON NAME:** Mesotrione

**TEST MATERIAL PURITY:** >98.1 %

**IUPAC NAME:** 2-[4-(Methylsulfonyl)-2-nitrobenzoyl]cyclohexane-1,3-dione

**SYNONYMS:** ZA1296;

**END-USE PRODUCT:**

Reference	MRID
(1995) ZA1296: Whole body autoradiography study in the rat following a single oral dose (mg/kg). Central Toxicology Laboratory, Cheshire, UK. Laboratory Report/Study No. CTL/P/4666/PR0990, September 19, 1995. Unpublished.	44505101
(1996) ZA1296: Excretion and tissue retention of a single oral dose (100 mg/kg) in the rat. Central Toxicology Laboratory, Cheshire, UK. Laboratory Report/Study No. CTL/P/4927/UR0501, May 17, 1996. Unpublished.	44505102
(1996) ZA1296: Biotransformation in the rat. Central Toxicology Laboratory, Cheshire, UK. Laboratory Report/Study No. CTL/P/4930/UR0442, June 3, 1996. Unpublished.	44505103
(1996) ZA1296: Excretion and tissue retention of a single oral dose (1 mg/kg) in the rat. Central Toxicology Laboratory, Cheshire, UK. Laboratory Report/Study No. CTL/P/4948/UR0502, May 20, 1996. Unpublished.	44505104
(1996) ZA1296: Excretion and tissue retention of a single intravenous dose (1 mg/kg) in the rat. Central Toxicology Laboratory, Cheshire, UK. Laboratory Report/Study No. CTL/P/4976/UR0522, May 29, 1996. Unpublished.	44505105
(1996) ZA.1296: Excretion and tissue retention of a single oral dose (1 mg/kg) in the rat following repeat dosing. Central Toxicology Laboratory, Cheshire, UK. Laboratory Report/Study No. CTL/P/4995/UR0525, May 24, 1996. Unpublished.	44505106

# Go To Live Demo

C:\Users\rkolancz\Documents\UnnamedDER.xml - DER Composer

DER Composer v5.2 (Rat/Livestock)  
Developed by LMC/Bourgas in Collaboration with US EPA/ORD/MERL-NHEERL

I. General info II. Materials and methods III. Results IV. Discussion and conclusions V. Appendix VI. Attachments

Header

**EPA REVIEWER:**  *Signature*  
[Insert Branch], Health Effects Division (7509C) **DATE:** 4/13/2021

**EPA SECONDARY REVIEWER:**  *Signature*  
[Insert Branch], Health Effects Division (7509C) **DATE:** 4/13/2021

**EPA WAM:**  *Signature*  
[Insert Branch], Health Effects Division (7509C) **DATE:** 4/13/2021

**TXR#:**

**DATA EVALUATION RECORD**

**STUDY TYPE:** Nature of the Residues in Animals - Lactating goat; DACO 6.2 / OCSPP 860.1300/OECD II6.2.2, 6.2.3 & IIIA 8.2, 8.4.1, 8.4.2

**AGENCY CODE:** US EPA PC CODE      
Code type Code value

**DP BARCODE:**   
**SUBMISSION NO:**

**TEST MATERIAL COMMON NAME:** Place common name (company experimental name) here

**TEST MATERIAL PURITY:**  %

**IUPAC NAME:**

**CAS NAME:**

**SYNONYMS:**

**END-USE PRODUCT:**

**CITATION**  
+

Reference MRID

Livestock

11:13 AM 4/13/2021

Transition Back to Juan to finish

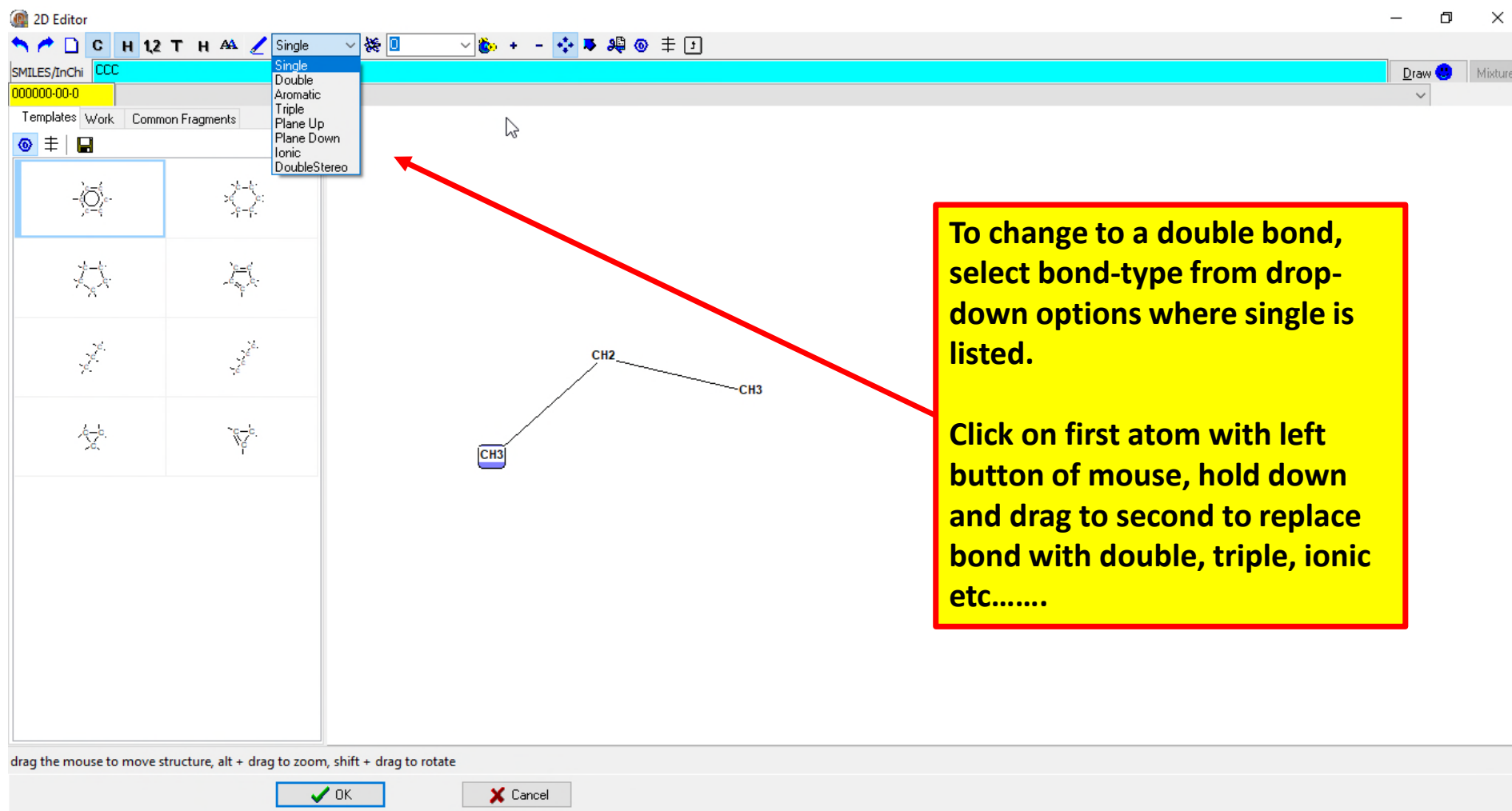


- **Drawing Tools**
- **Structure Editor**

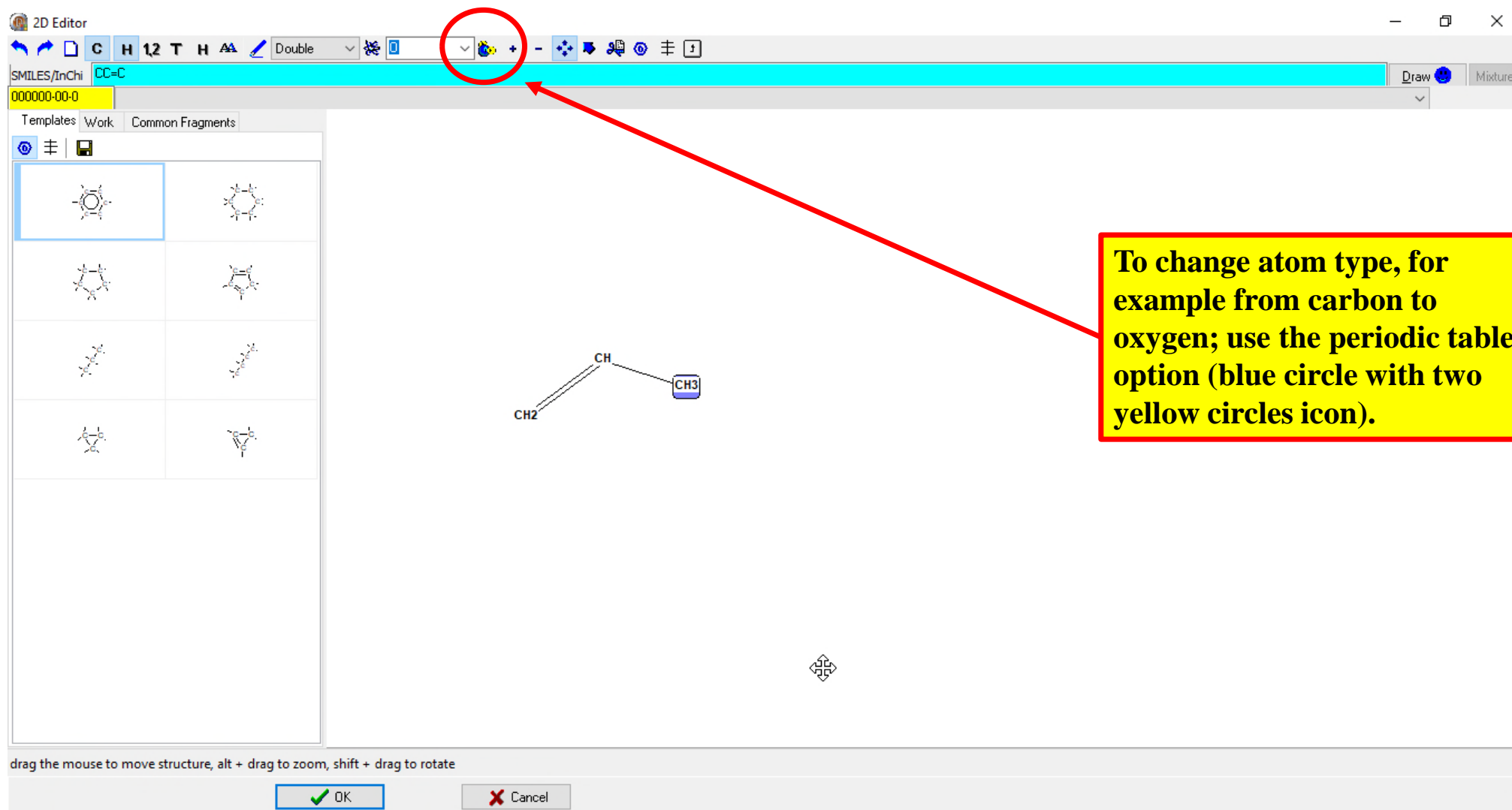


# STRUCTURE EDITING

The following screen-shots illustrate some other functions of the STRUCTURE DRAWING package that may be used to modify/edit/draw 2-D structures of parent/metabolites.



To change atom type, for example from carbon to oxygen; use the periodic table option (blue circle with two yellow circles icon).



To change atom type, for example from carbon to oxygen; use the periodic table option (blue circle with two yellow circles icon).

The table opens, click on atom choice, click yes to accept choice and the table goes away.

2D Editor

SMILES/InChi CC=C

000000-00-0

Templates Work Common Fragments

Periodic Table

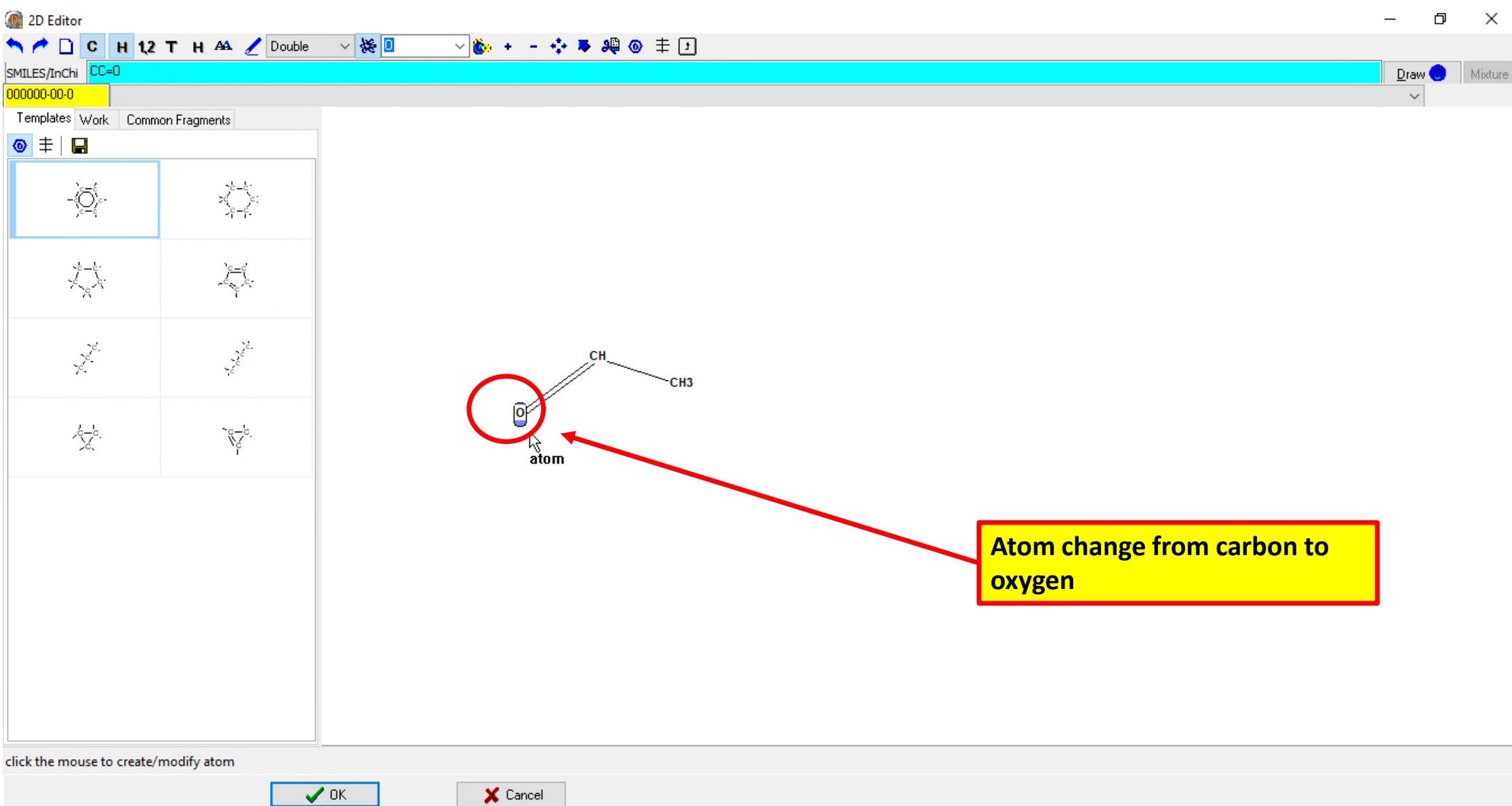
1 H																	2 He				
3 Li	4 Be															5 B	6 C	7 N	8 O	9 F	10 Ne
11 Na	12 Mg															13 Al	14 Si	15 P	16 S	17 Cl	18 Ar
19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr				
37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe				
55 Cs	56 Ba	57 *La	72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 Pt	79 Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rn				
87 Fr	88 Ra	89 +Ac																			
58 Ce	59 Pr	60 Nd	61 Pm	62 Sm	63 Eu	64 Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb	71 Lu								
90 Th	91 Pa	92 U	93 Np	94 Pu	95 Am	96 Cm	97 Bk	98 Cf	99 Es	100 Fm	101 Md	102 No	103 Lr								

Selected element: O

☐ Labeled  
Number:

drag the mouse to move structure, alt + drag to zoom, shift + drag to rotate

**Simply click on the atom in the structure that you wish to replace and the substitution will be made.**



2D Editor

SMILES/InChi S\_c1ccccc1

000000-00-0

Templates Work Common Fragments

The atomic symbol icon allows for placement of a single atom.

The benzene ring icon allows you to put an aromatic ring on the drawing.

The screenshot shows the 2D Editor software interface. At the top, the title bar reads '2D Editor'. Below it, a toolbar contains various icons for drawing and editing. Two icons are circled in red: the 'Add Atom' icon (a blue circle with a white 'S') and the 'Add Aromatic Ring' icon (a benzene ring). The 'SMILES/InChi' field displays the string S\_c1ccccc1. Below this, a 'Templates' panel shows a grid of chemical structures. The first structure in the grid is a benzene ring, which is highlighted with a blue border. A red arrow points from a yellow text box to this icon. Another red arrow points from a second yellow text box to the 'Add Aromatic Ring' icon in the toolbar. A third red arrow points from a third yellow text box to the 'Add Atom' icon. In the center of the drawing area, a small benzene ring with an 'S' atom attached is shown. To the right, a larger chemical structure is displayed, consisting of a benzene ring with an 'S' atom attached to one of the carbons. The bottom of the window features a status bar with 'OK' and 'Cancel' buttons, and a Windows taskbar at the very bottom showing the system clock as 1:12 PM on 2/17/2021.

click the mouse to create/modify atom

OK Cancel

oasis-lmc.org

1:12 PM  
2/17/2021

2D Editor

SMILES/InChi: 000000-00-0

Templates Work Common Fragments

OK Cancel

click/drag with: left button to select; right button to move

The scissors icon is the delete or cut feature.

The four arrow icon allows you to move the structure.

Ionic structures may be represented with + and - charges.

Templates for common structures may be created, stored and recalled for future use.

The screenshot shows the 2D Editor software interface. At the top, there is a toolbar with various icons. Three icons are circled in red: a plus sign, a minus sign, and a scissors icon. Red arrows point from these icons to yellow text boxes. The scissors icon is labeled 'The scissors icon is the delete or cut feature.' The four arrow icon is labeled 'The four arrow icon allows you to move the structure.' The plus and minus icons are labeled 'Ionic structures may be represented with + and - charges.' On the left side, there is a 'Templates' panel with a grid of chemical structures. A red arrow points from one of the structures in the grid to a yellow text box that says 'Templates for common structures may be created, stored and recalled for future use.' At the bottom, there is a status bar with 'OK' and 'Cancel' buttons, and a message 'click/drag with: left button to select; right button to move'. The Windows taskbar is visible at the very bottom.



Once a structure is drawn, the SMILES string will be auto-generated for that structure.

