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).

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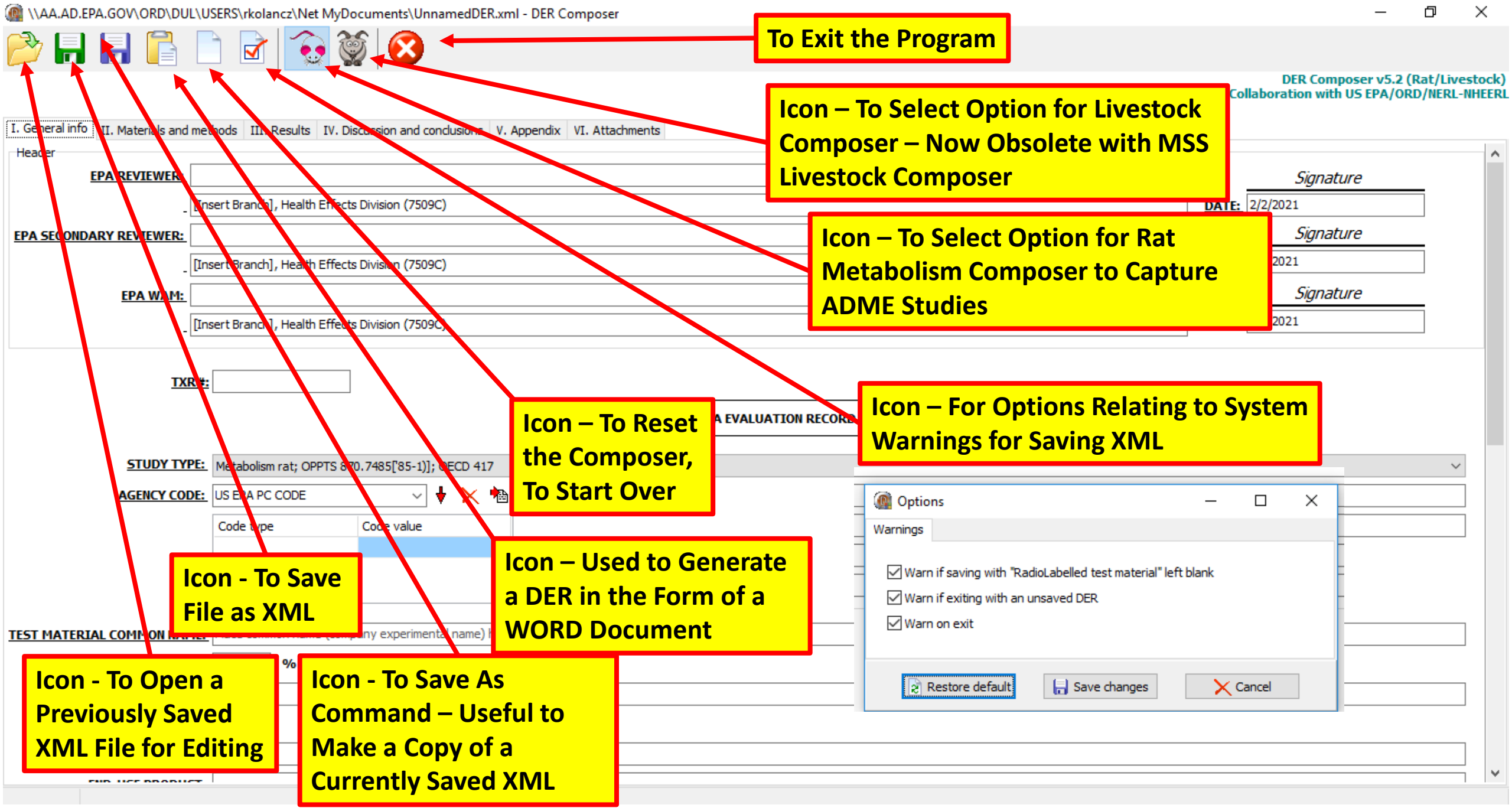
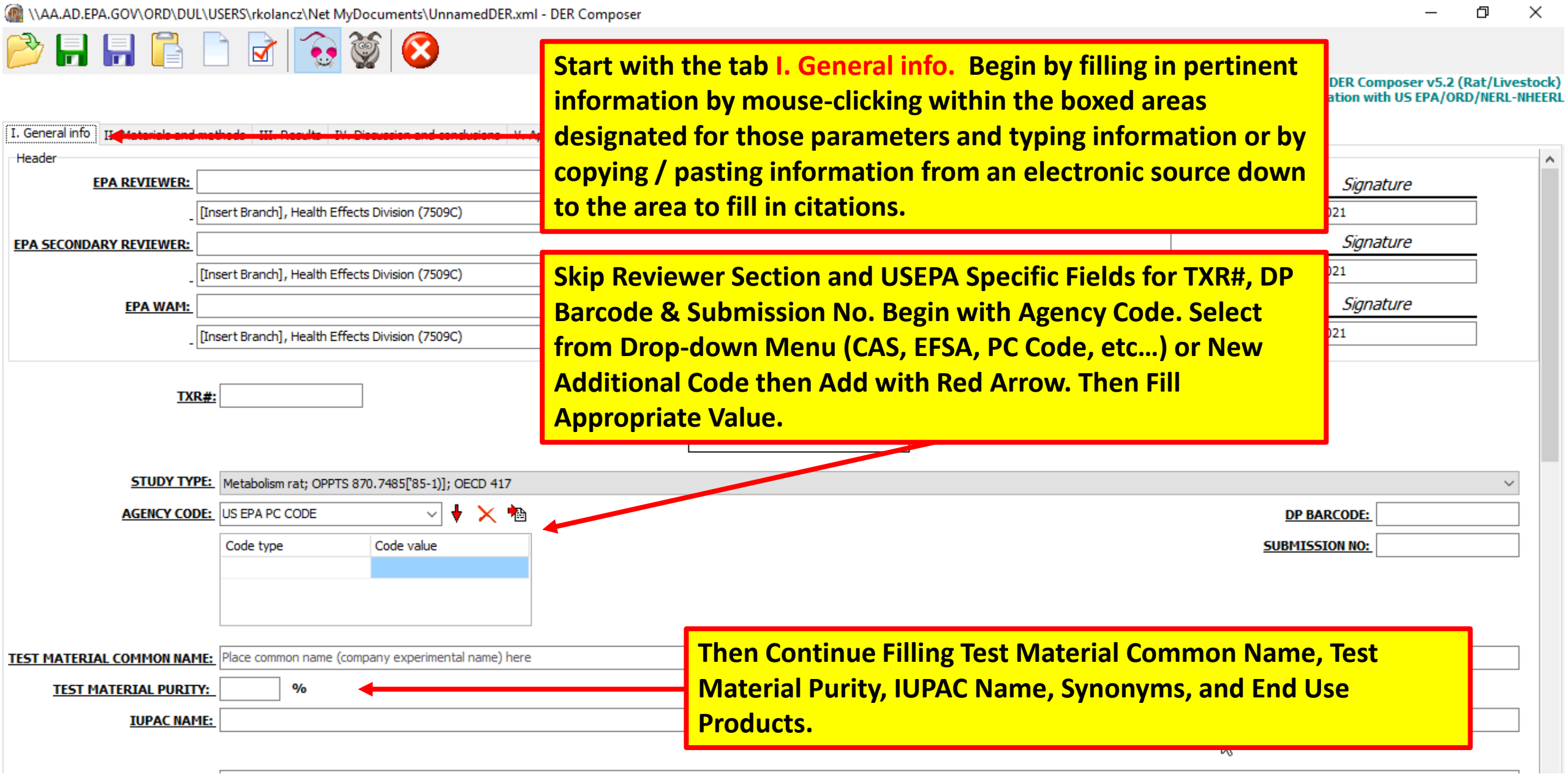
Center for Computational Toxicology and Exposure
Office of Research and Development, U.S. Environmental Protection Agency
Duluth, MN, USA

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

Open the program – start up will appear as follows:



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.

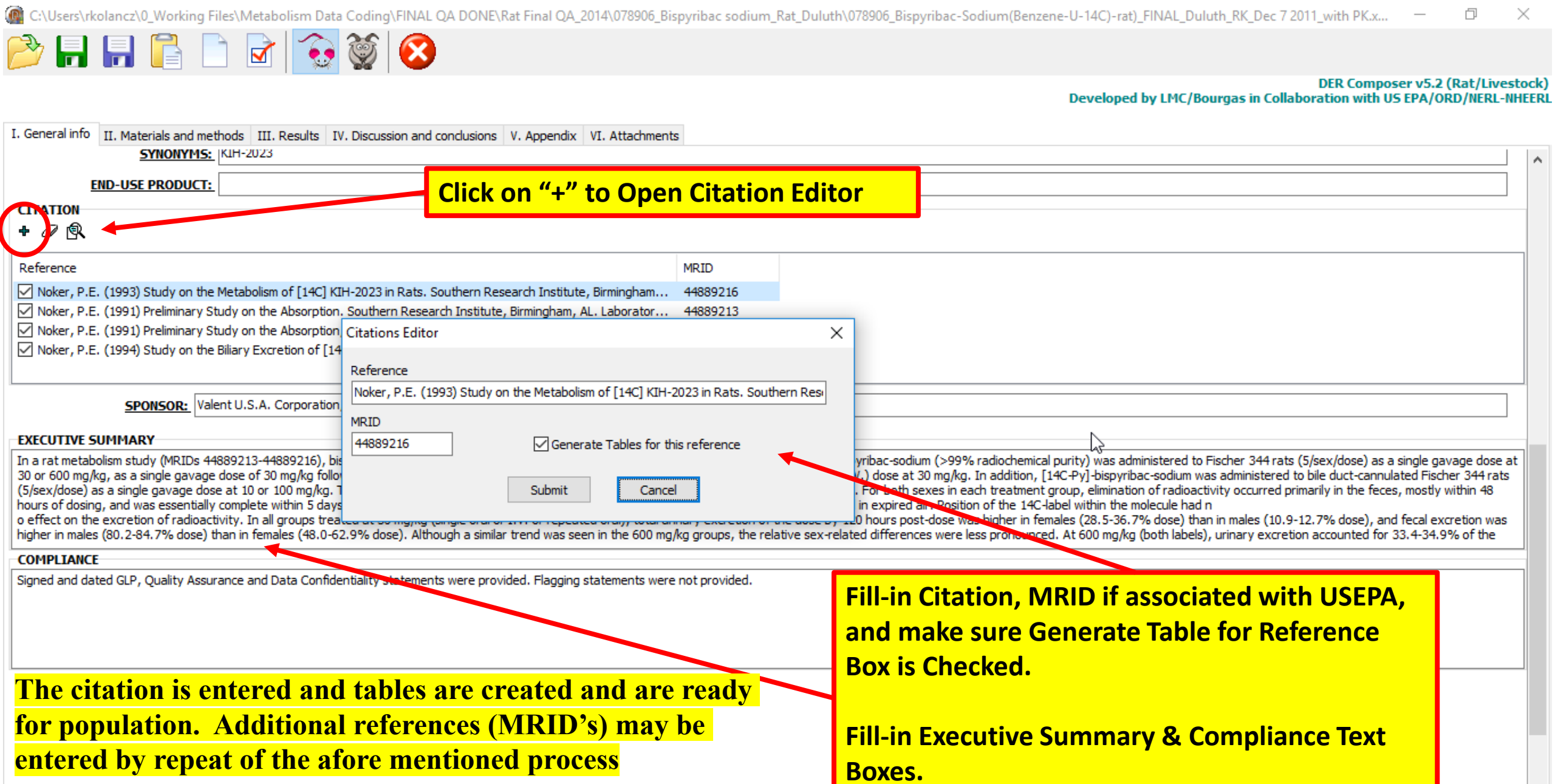


Start with the tab I. General info. Begin by filling in pertinent information by mouse-clicking within the boxed areas designated for those parameters and typing information or by copying / pasting information from an electronic source down to the area to fill in citations.

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.

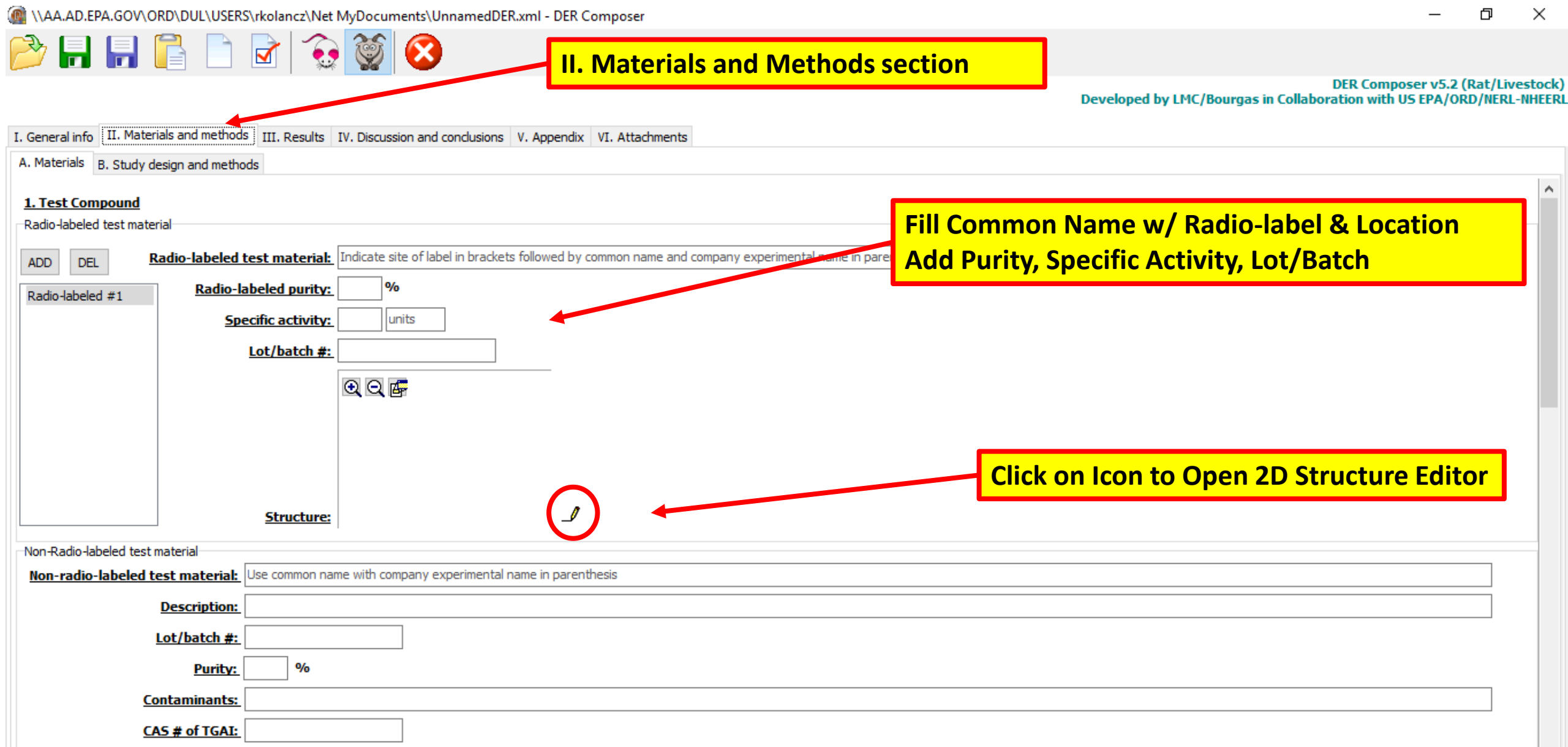


The citation is entered and tables are created and are ready for population. Additional references (MRID's) may be entered by repeat of the afore mentioned process

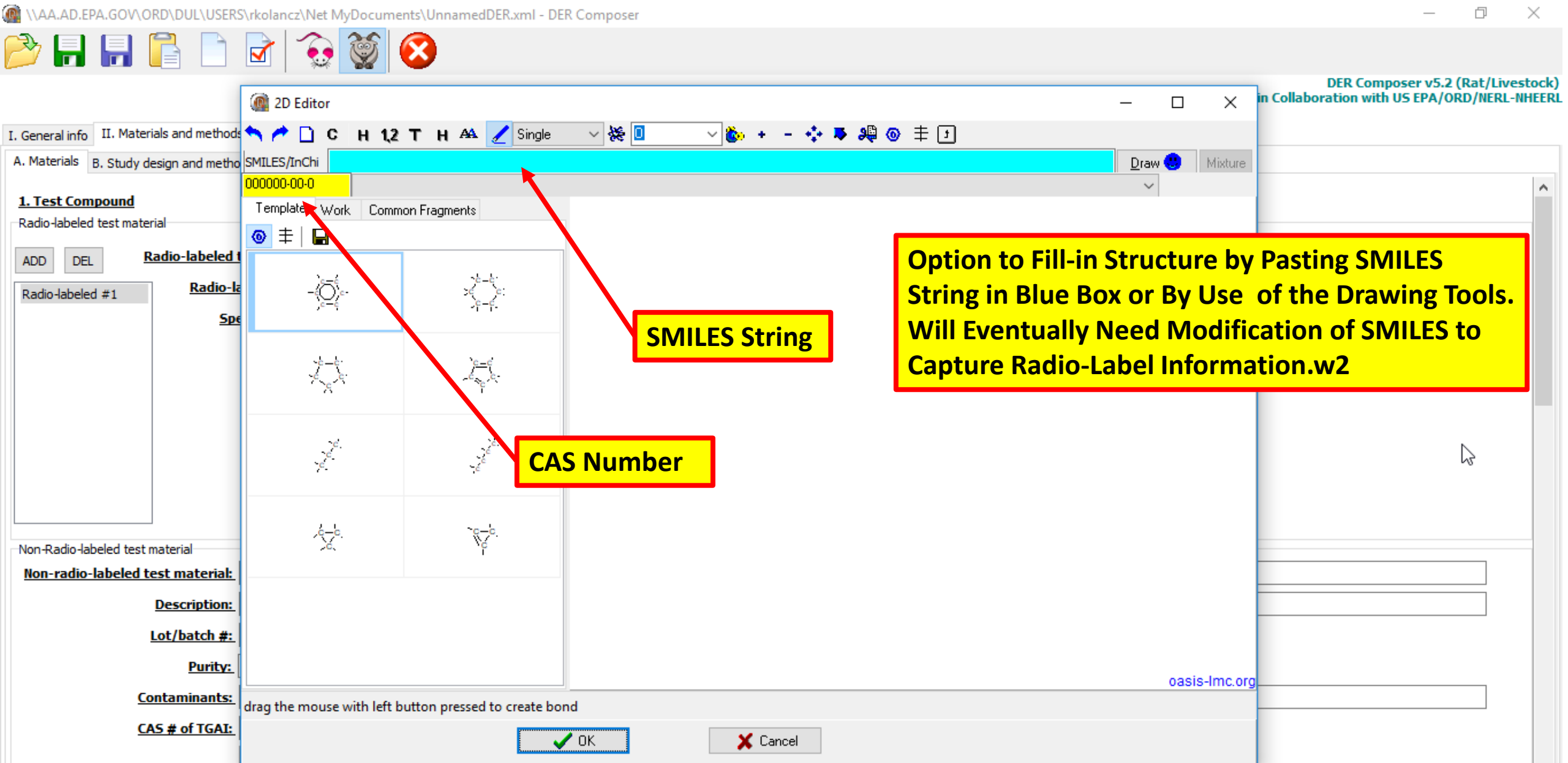
Fill-in Citation, MRID if associated with USEPA, and make sure Generate Table for Reference Box is Checked.

Fill-in Executive Summary & Compliance Text Boxes.

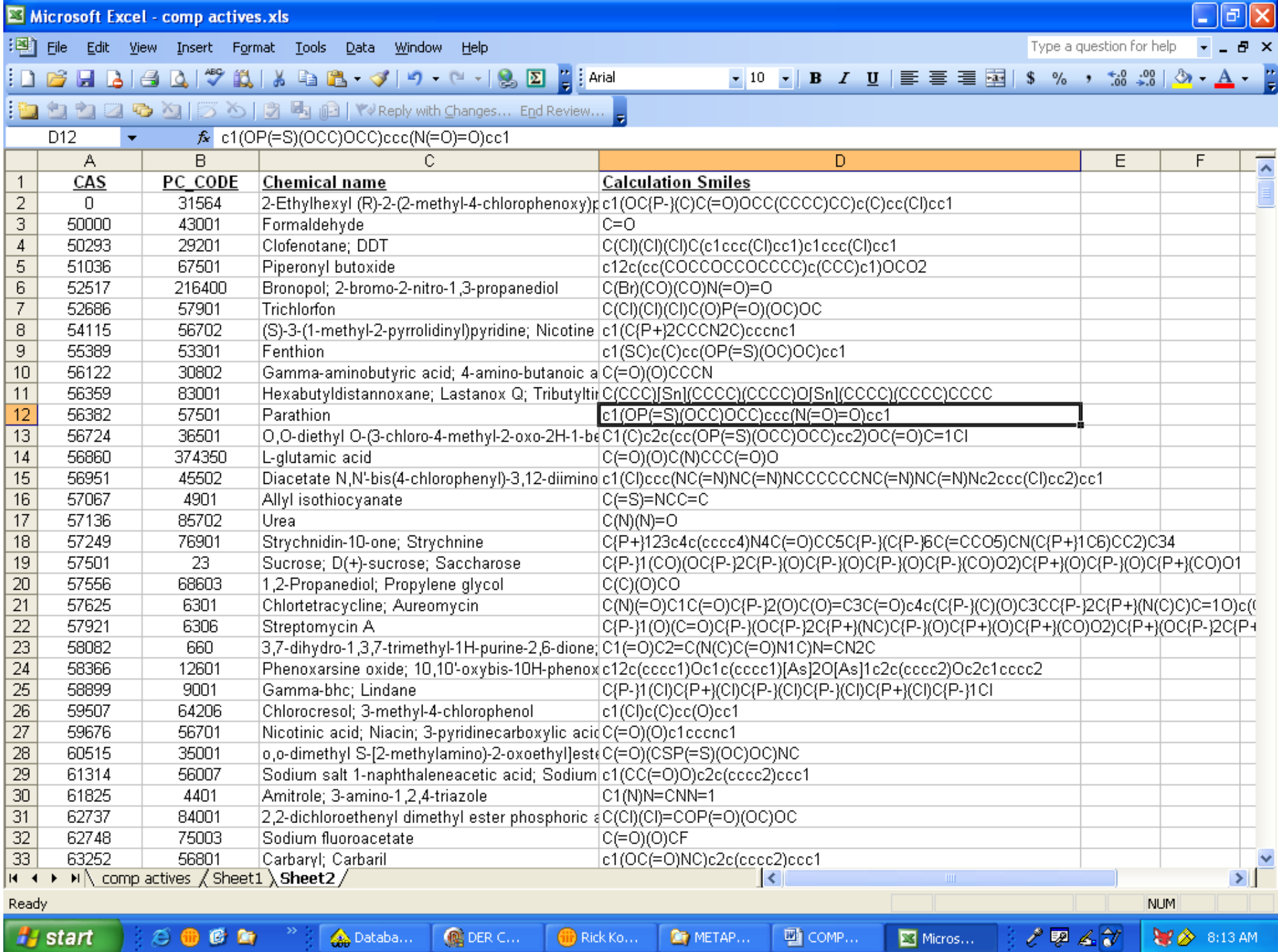
Next the tab II. Materials and methods and sub-tab A. Materials may be populated. Data is filled in via directly typing or copy/paste from electronic documents until reaching the structure entry. To enter the Radio-labeled Test Material and Non-radio-labeled Test Material structures:



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.



To get started a list of parent 2-D structures represented as linear "SMILES strings" will be made available. Locate the appropriate structure from the excel file, copy the SMILES string.



Microsoft Excel - comp actives.xls

File Edit View Insert Format Tools Data Window Help

Type a question for help

Arial 10

Reply with Changes... End Review...

D12 c1(OP(=S)(OCC)OCC)ccc(N(=O)=O)cc1

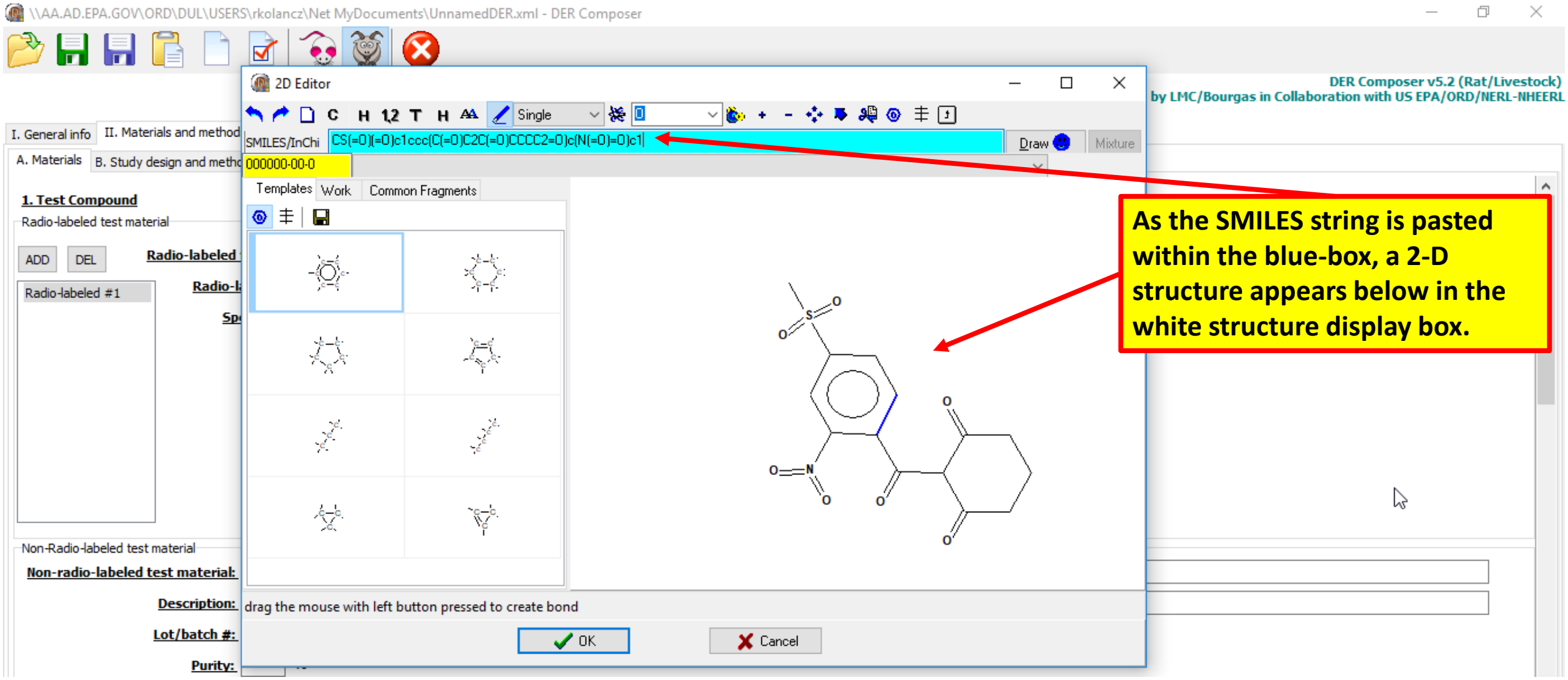
	A	B	C	D	E	F
1	CAS	PC_CODE	Chemical name	Calculation Smiles		
2	0	31564	2-Ethylhexyl (R)-2-(2-methyl-4-chlorophenoxy)p	c1(OC(P-)(C)C(=O)OCC(CCCC)CC)c(C)cc(Cl)cc1		
3	50000	43001	Formaldehyde	C=O		
4	50293	29201	Clofenotane; DDT	C(Cl)(Cl)(Cl)C(c1ccc(Cl)cc1)c1ccc(Cl)cc1		
5	51036	67501	Piperonyl butoxide	c12c(cc(COCCOCCOCCCC)c(CCC)c1)OCO2		
6	52517	216400	Bronopol; 2-bromo-2-nitro-1,3-propanediol	C(Br)(CO)(CO)N(=O)=O		
7	52686	57901	Trichlorfon	C(Cl)(Cl)(Cl)C(O)P(=O)(OC)OC		
8	54115	56702	(S)-3-(1-methyl-2-pyrrolidinyl)pyridine; Nicotine	c1(C{P+}2CCCN2C)cccnc1		
9	55389	53301	Fenthion	c1(SC)c(C)cc(OP(=S)(OC)OC)cc1		
10	56122	30802	Gamma-aminobutyric acid; 4-amino-butanoic a	C(=O)(O)CCCN		
11	56359	83001	Hexabutyldistannoxane; Lastanox Q; Tributyltir	C(CCC)[Sn](CCCC)(CCCC)O[Sn](CCCC)(CCCC)CCCC		
12	56382	57501	Parathion	c1(OP(=S)(OCC)OCC)ccc(N(=O)=O)cc1		
13	56724	36501	O,O-diethyl O-(3-chloro-4-methyl-2-oxo-2H-1-be	C1(C)c2c(cc(OP(=S)(OCC)OCC)cc2)OC(=O)C=1Cl		
14	56860	374350	L-glutamic acid	C(=O)(O)C(N)CCC(=O)O		
15	56951	45502	Diacetate N,N'-bis(4-chlorophenyl)-3,12-diimino	c1(Cl)ccc(NC(=N)NC(=N)NCCCCCCNC(=N)NC(=N)Nc2ccc(Cl)cc2)cc1		
16	57067	4901	Allyl isothiocyanate	C(=S)=NCC=C		
17	57136	85702	Urea	C(N)(N)=O		
18	57249	76901	Strychnidin-10-one; Strychnine	C{P+}123c4c(cccc4)N4C(=O)CC5C{P-}(C{P-}6C(=CCO5)CN(C{P+}1C6)CC2)C34		
19	57501	23	Sucrose; D(+)-sucrose; Saccharose	C{P-}1(CO)(OC{P-}2C{P-}(O)C{P-}(O)C{P-}(O)C{P-}(CO)O2)C{P+}(O)C{P-}(O)C{P+}(CO)O1		
20	57556	68603	1,2-Propanediol; Propylene glycol	C(C)(O)CO		
21	57625	6301	Chlortetracycline; Aureomycin	C(N)(=O)C1C(=O)C{P-}2(O)C(O)=C3C(=O)c4c(C{P-}(C)(O)C3CC{P-}2C{P+}(N(C)C)C=1O)c(		
22	57921	6306	Streptomycin A	C{P-}1(O)(C=O)C{P-}(OC{P-}2C{P+}(NC)C{P-}(O)C{P+}(O)C{P+}(CO)O2)C{P+}(OC{P-}2C{P+		
23	58082	660	3,7-dihydro-1,3,7-trimethyl-1H-purine-2,6-dione;	C1(=O)C2=C(N(C)C(=O)N1C)N=CN2C		
24	58366	12601	Phenoxarsine oxide; 10,10'-oxybis-10H-phenox	c12c(cccc1)Oc1c(cccc1)[As]2O[As]1c2c(cccc2)Oc2c1cccc2		
25	58899	9001	Gamma-bhc; Lindane	C{P-}1(Cl)C{P+}(Cl)C{P-}(Cl)C{P-}(Cl)C{P+}(Cl)C{P-}1Cl		
26	59507	64206	Chlorocresol; 3-methyl-4-chlorophenol	c1(Cl)c(C)cc(O)cc1		
27	59676	56701	Nicotinic acid; Niacin; 3-pyridinecarboxylic acid	C(=O)(O)c1cccnc1		
28	60515	35001	o,o-dimethyl S-[2-methylamino)-2-oxoethyl]este	C(=O)(CSP(=S)(OC)OC)NC		
29	61314	56007	Sodium salt 1-naphthaleneacetic acid; Sodium	c1(CC(=O)O)c2c(cccc2)ccc1		
30	61825	4401	Amitrole; 3-amino-1,2,4-triazole	C1(N)N=CNN=1		
31	62737	84001	2,2-dichloroethenyl dimethyl ester phosphoric a	C(Cl)(Cl)=COP(=O)(OC)OC		
32	62748	75003	Sodium fluoroacetate	C(=O)(O)CF		
33	63252	56801	Carbaryl; Carbaril	c1(OC(=O)NC)c2c(cccc2)ccc1		

comp actives Sheet1 Sheet2

Ready NUM

start Databa... DER C... Rick Ko... METAP... COMP... Micros... 8:13 AM

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.

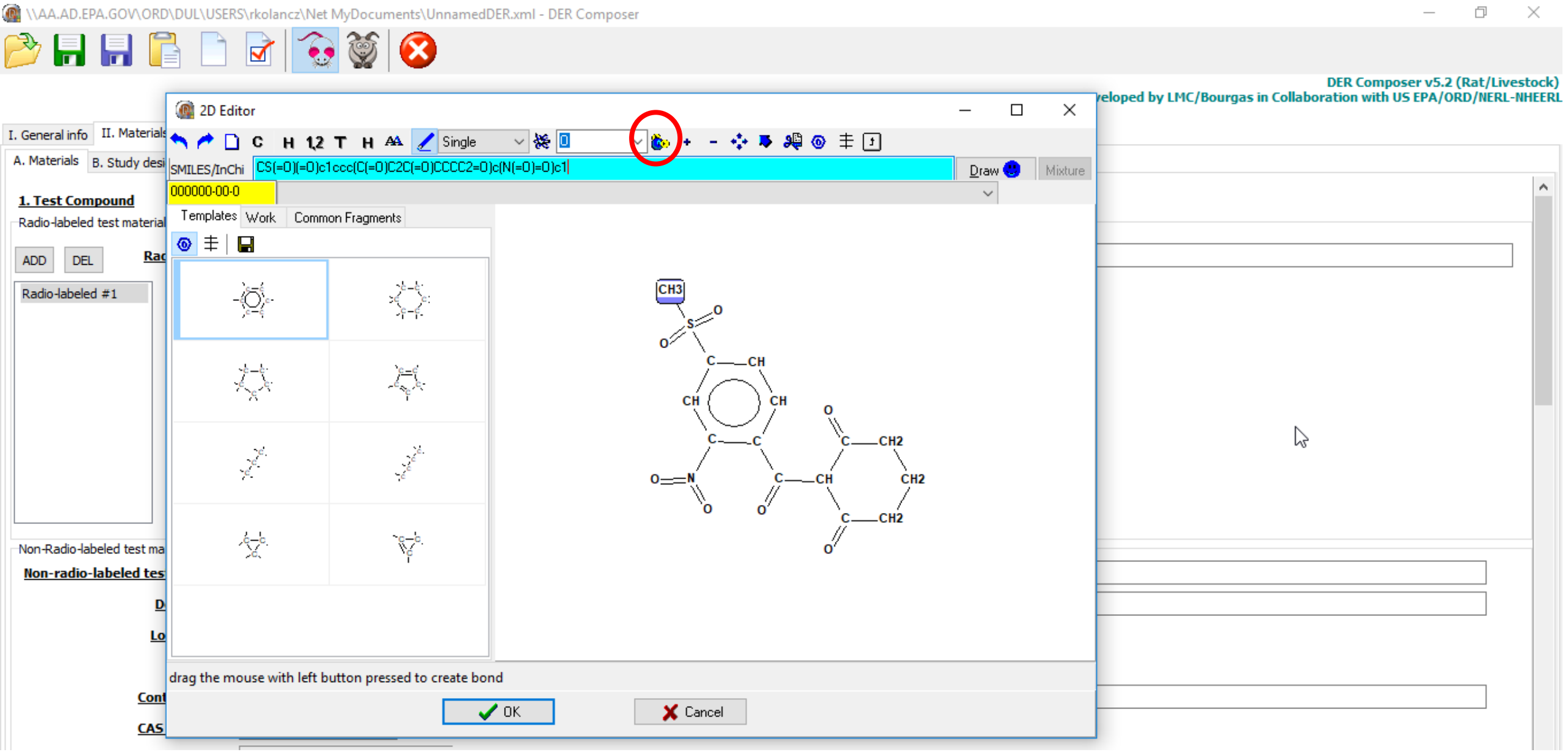


As the SMILES string is pasted within the blue-box, a 2-D structure appears below in the white structure display box.

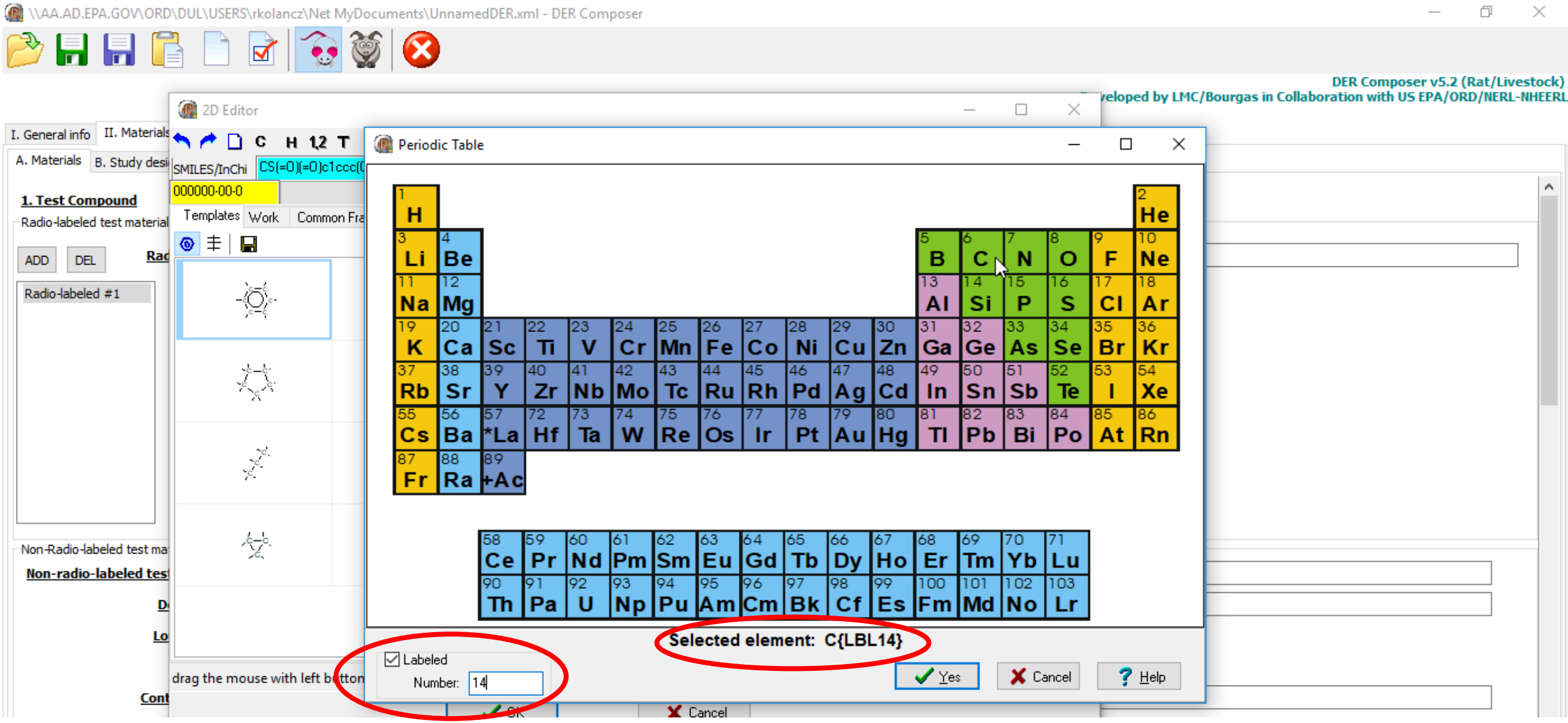
The parent structure (now present in the STRUCTURE DRAWING editor) may be modified utilizing tools within the editor. Specifically a label may be introduced in the structure of the radio-labeled parent.

Radio labeling of atoms

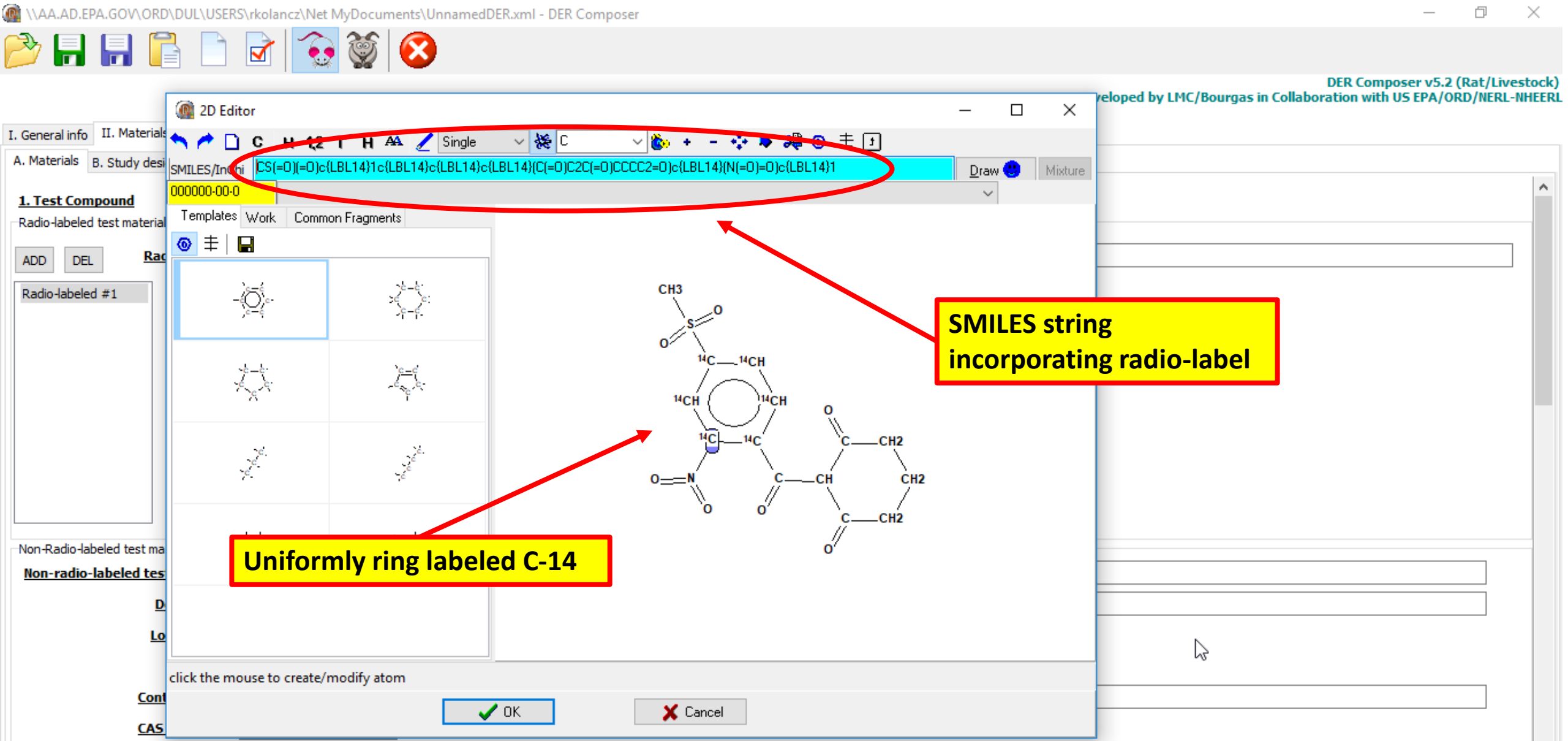
Within the STRUCTURE DRAWING window, open the periodic table by selecting the icon as circled in the figure below.



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.



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.



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

DER Composer v5.2 (Rat/Livestock)
Developed by LMC/Bourgas 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. Materials | B. Study design and methods

ADD DEL

Radio-labeled #1

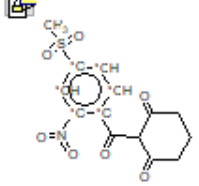
Radio-labeled test material: Mesotrione [14C-aromatic]

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

8:42 AM
2/17/2021

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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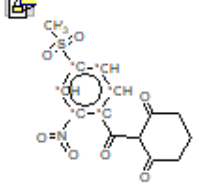
Lot/batch #: Y0684/159 or Y0684/011

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:

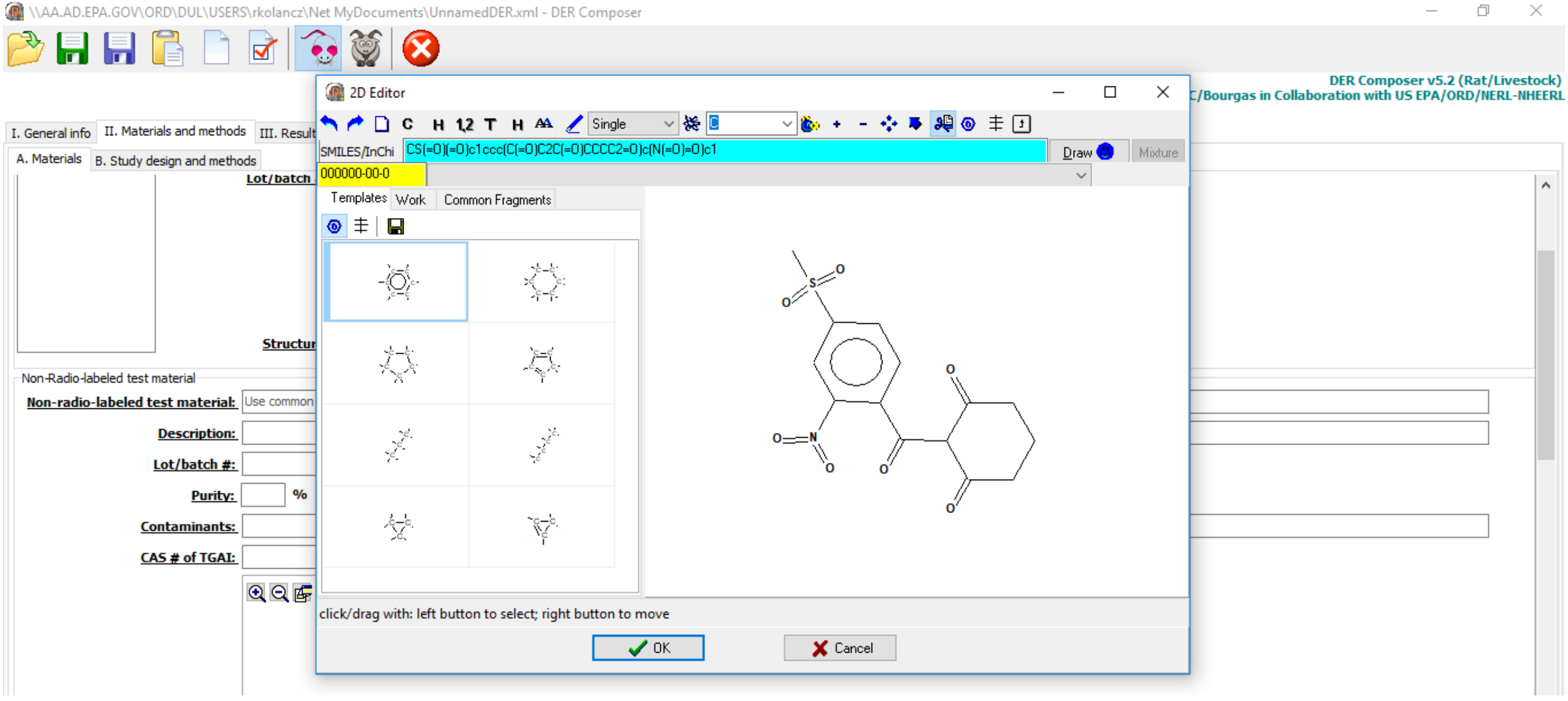
CAS # of TGAI:

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.



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

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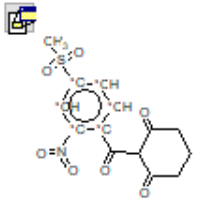
I. General info | II. Materials and methods | III. Results | IV. Discussion and conclusions | V. Appendix | VI. Attachments

A. Materials | B. Study design and methods

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

Structure:



Non-Radio-labeled test material

Non-radio-labeled test material: Mesotrione

Description: Cream solid or off-white powder

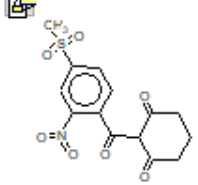
Lot/batch #: Y06684/008 or Y06684/005

Purity: >99.3 %

Contaminants: not specified

CAS # of TGAI: 104206-82-8

Structure:



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 #.

Physicochemical Properties

Parameter	Note	Value	Reference

Modified | Rat

9:04 AM
2/17/2021

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

DER Composer v5.2 (Rat/Livestock)
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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:APfSD

Age at study initiation: 7-9 weeks

Weight at study initiation: 175-300 g

Source: Biological Services Section or Barriered 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, Witham. Essex. UK). ad libitum, except for 10-1

Water: Tap water, ad libitum

Environmental conditions

Temperature: 21 ± 4 °C °C

Humidity: 30-70% %

Air changes: At least 12/hour

Photoperiod: 12-hr photoperiod

Acclimation period: 4 days

Fill-in Test Animal Fields

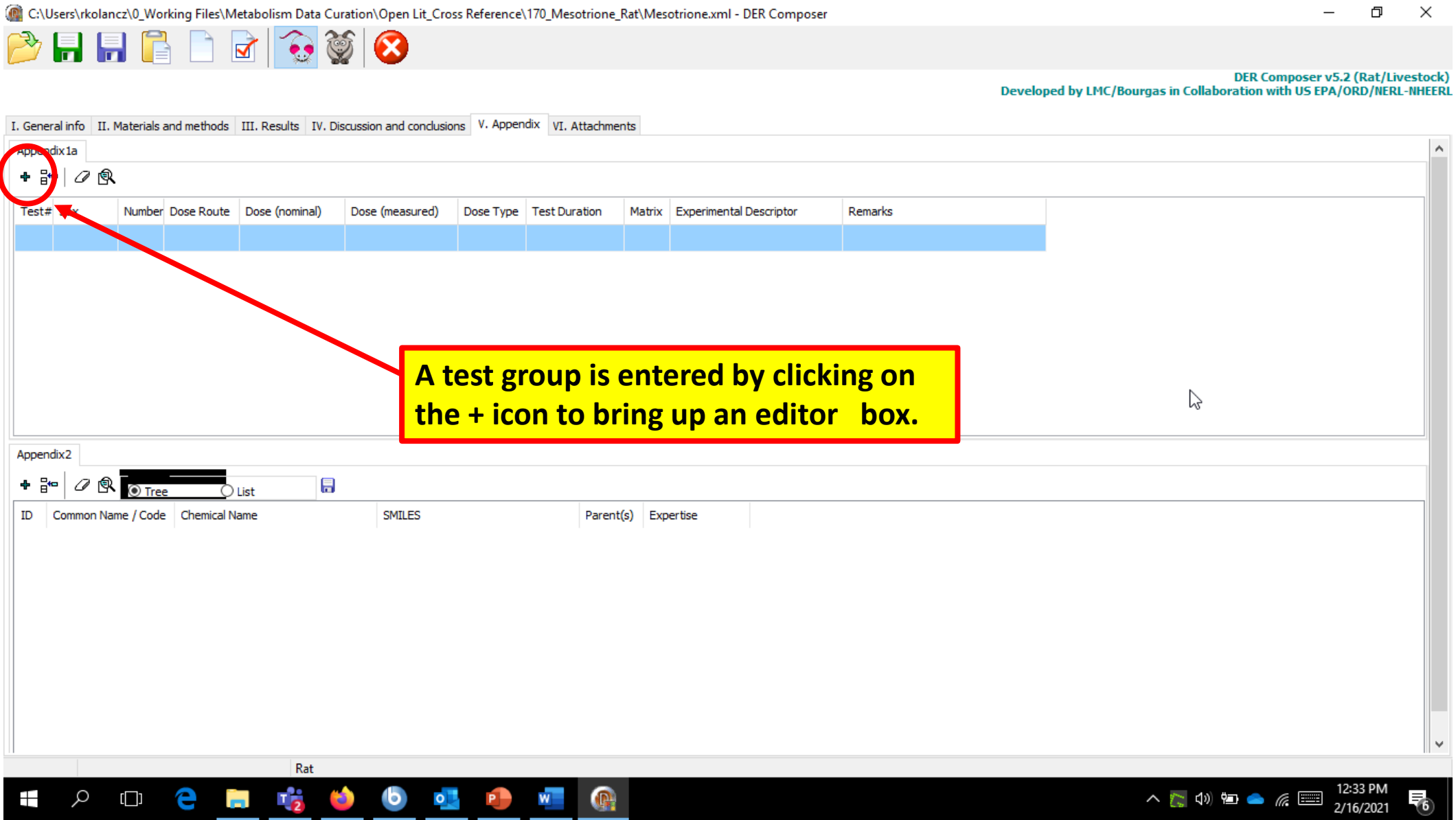
Fill-in Preparation of Dosing Solution

4. Preparation of dosing solutions

For the low-udose gioups, 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 chromotography. No results of these analyses were provided.

- **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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Appendix 1a

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

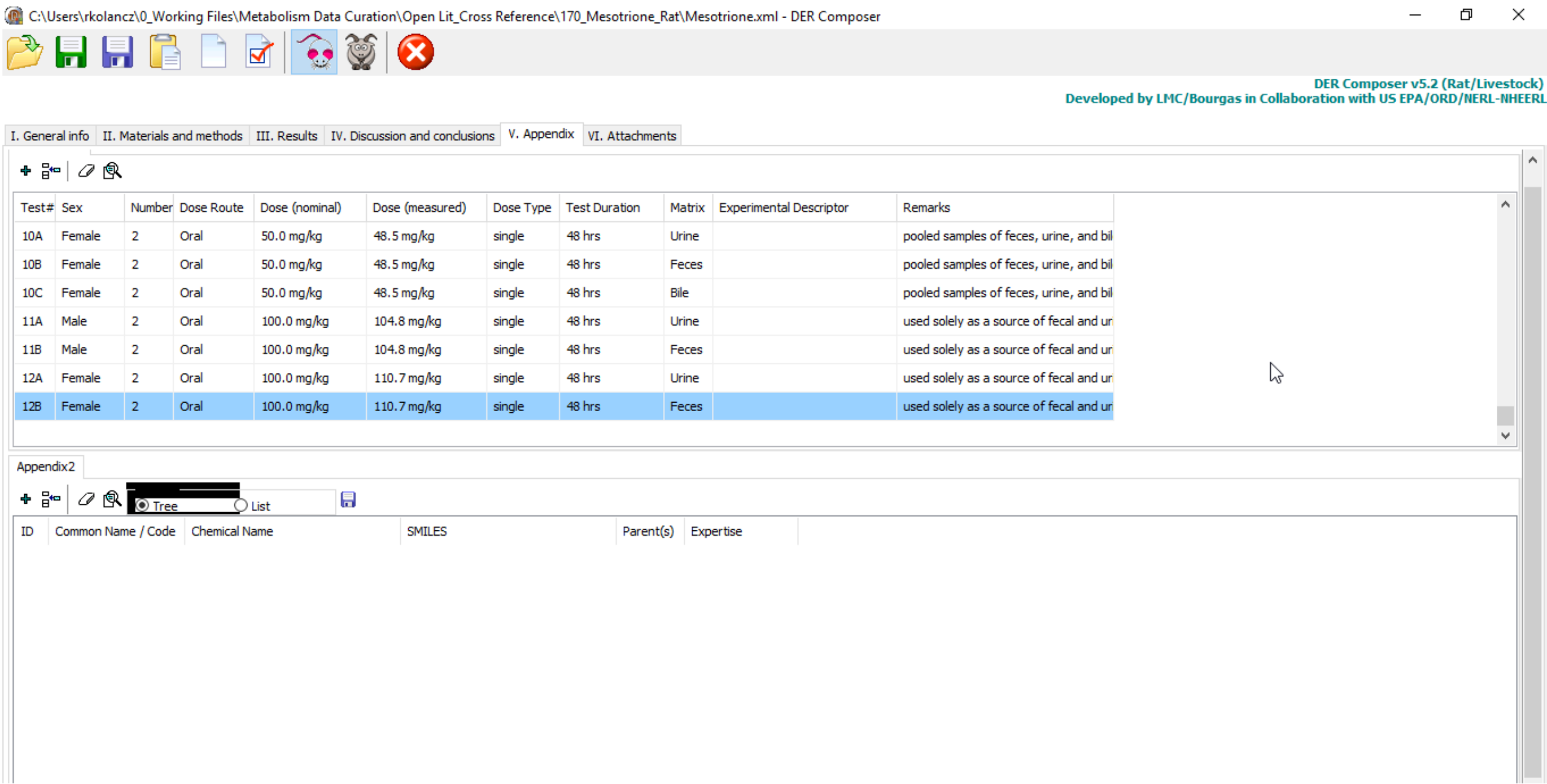
Tree | List

ID	Common Name / Code	Chemical Name	(s)	Expertise

Rat

12:58 PM
2/16/2021

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



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

DER Composer v5.2 (Rat/Livestock)
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A. Materials | B. Study design and methods

1. Group arrangements

Animals were assigned to the test groups noted in Table1

Table1a

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

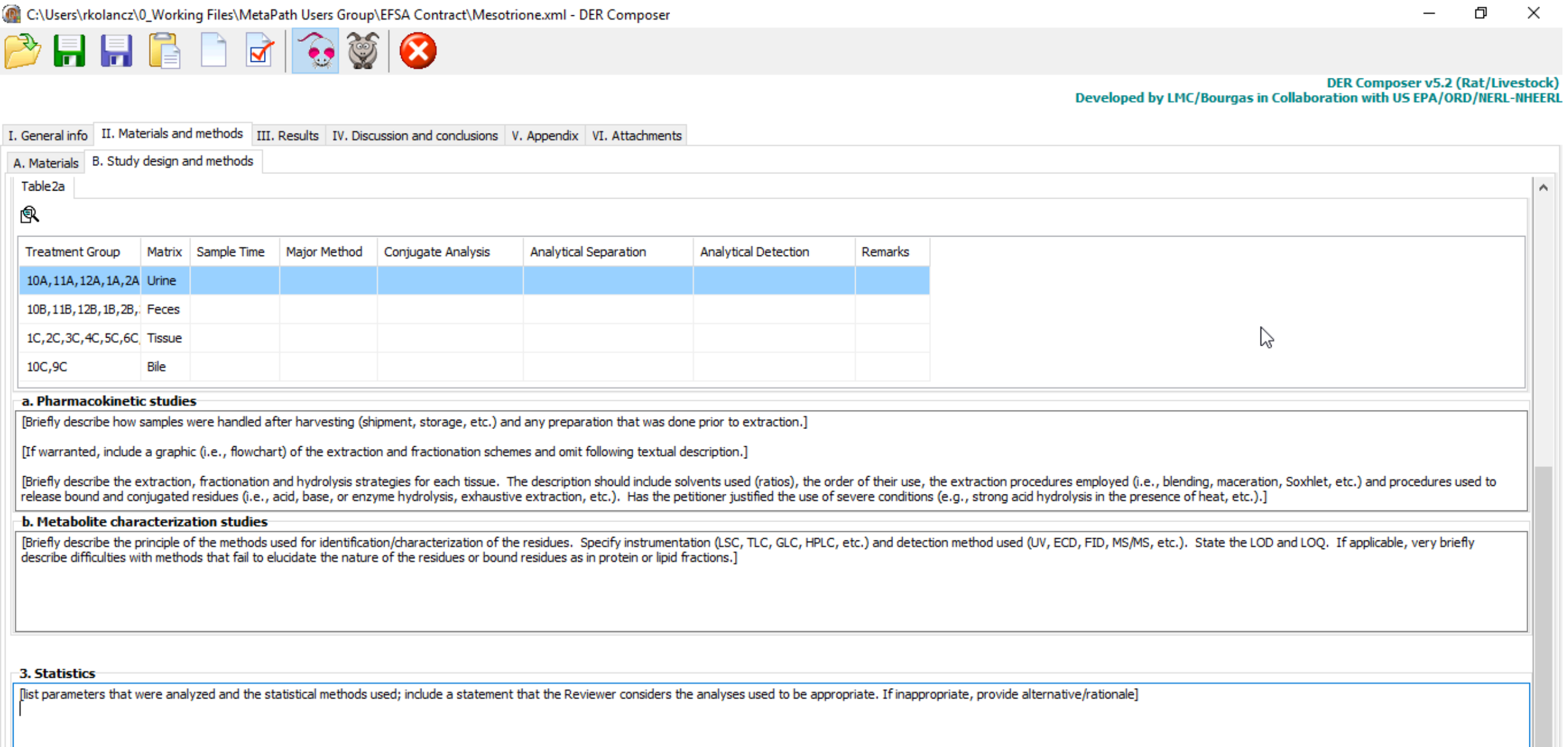
2. Dosing and sample collection

Briefly describe dosing methods and sample collection

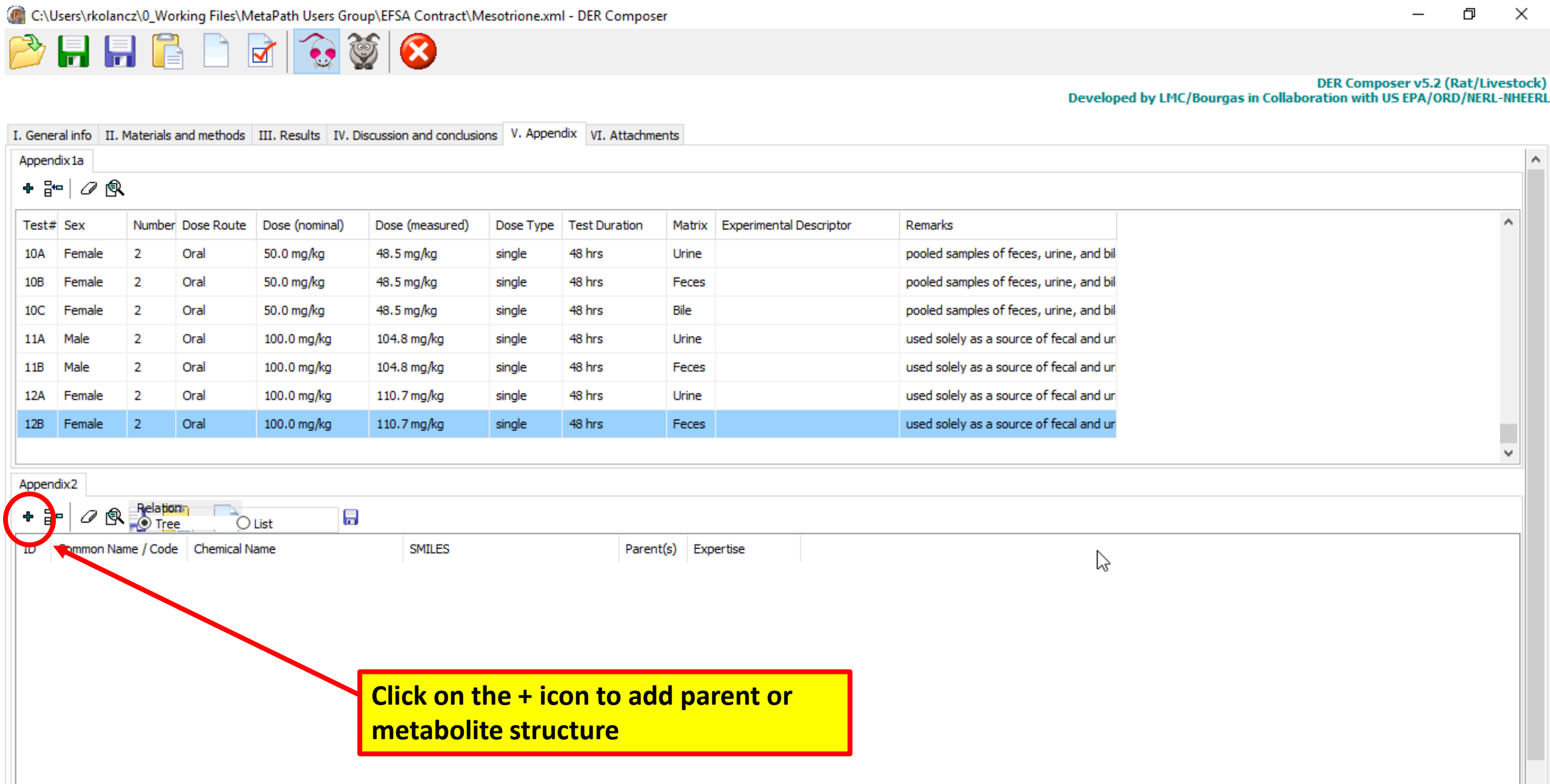
Table2a

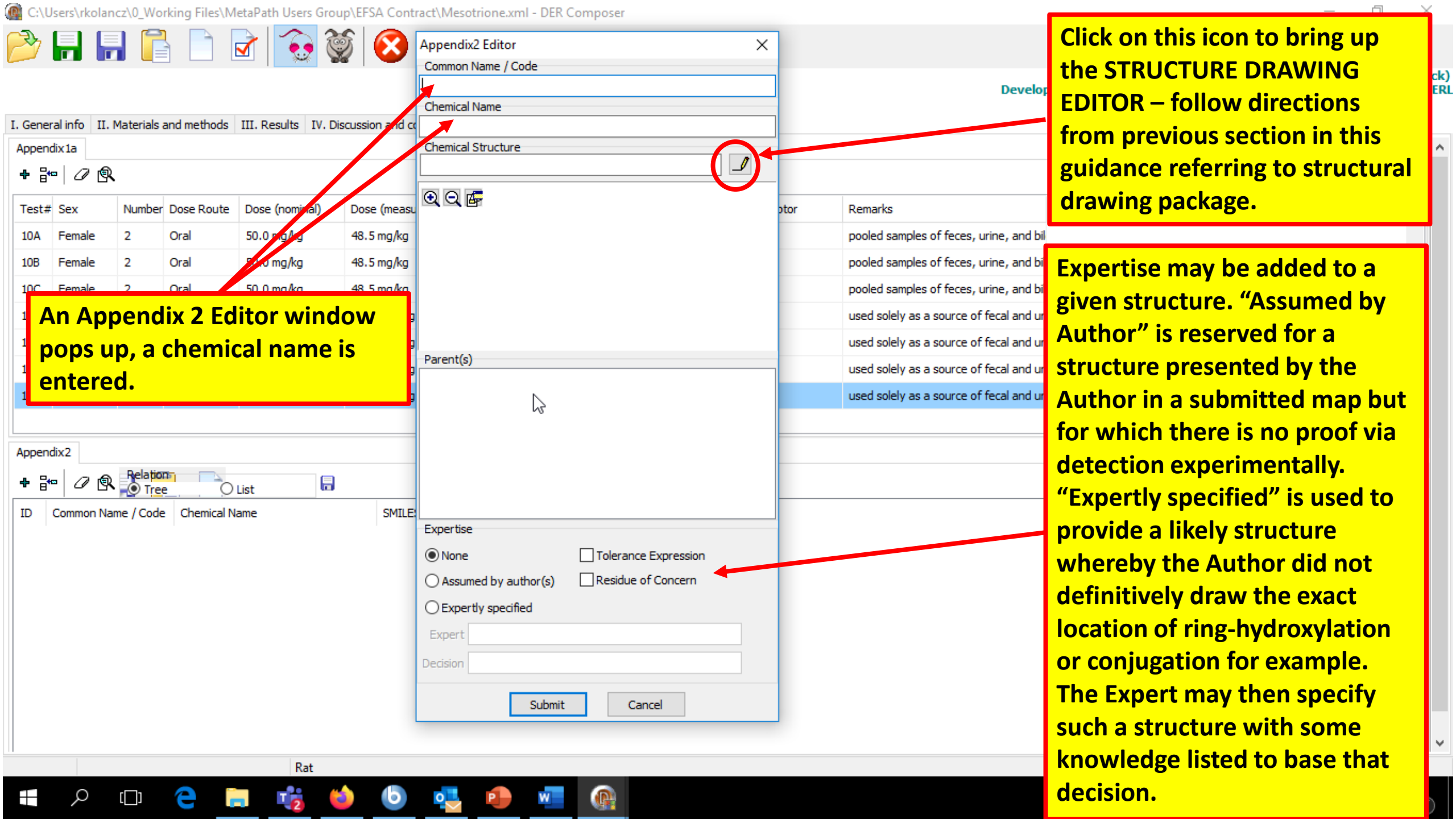
Treatment Group	Matrix	Sample Time	Major Method	Conjugate Analysis	Analytical Separation	Analytical Detection	Remarks

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.

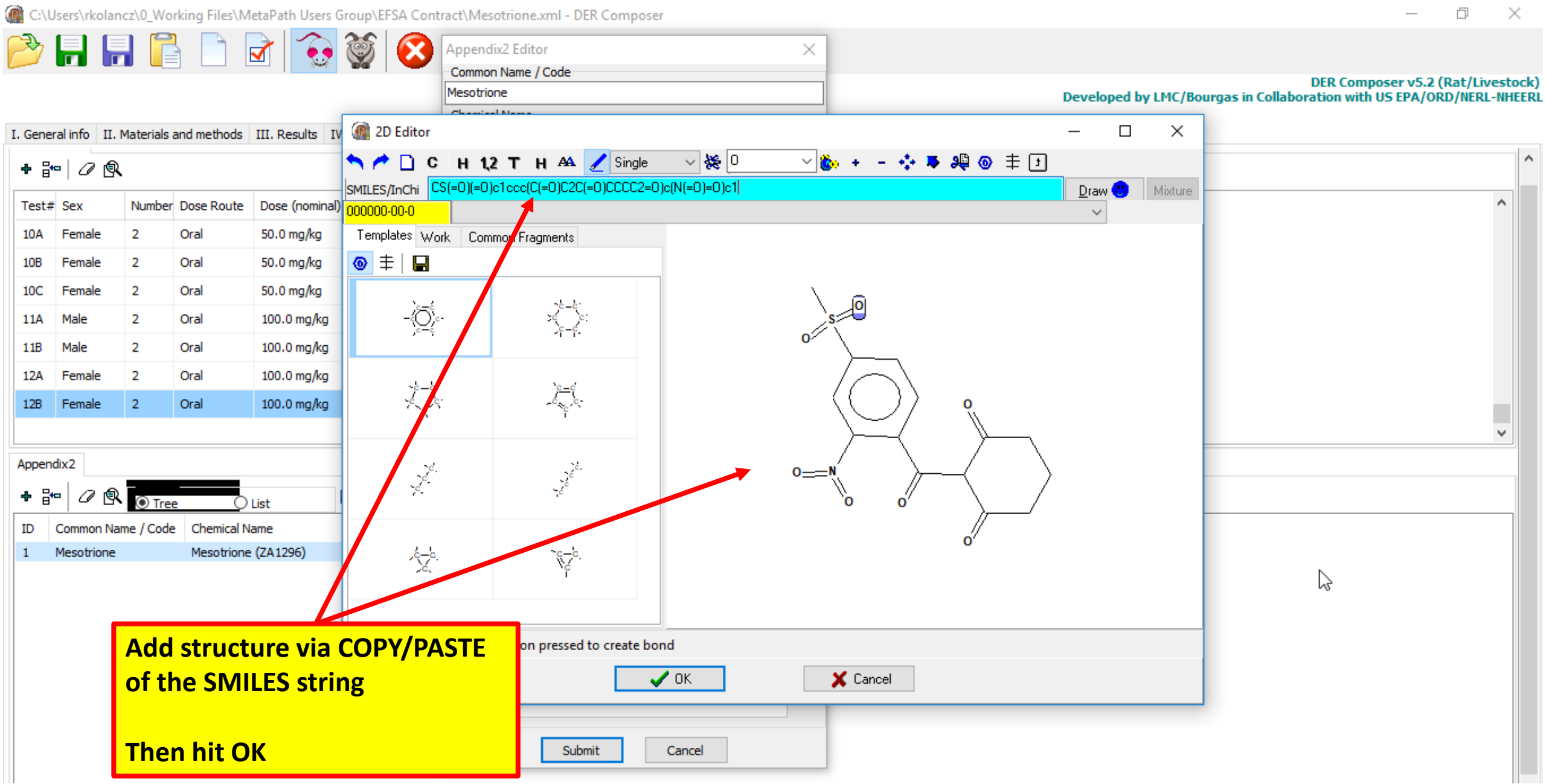


Next a Metabolite Inventory table should be completed as Appendix 2 of tab V. Appendix.




C:\Users\rkolancz\0_Working Files\MetaPath Users Group\EFSA Contract\Mesotrione.xml - DER Composer
Appendix2 Editor
Common Name / Code
Chemical Name
Chemical Structure
Parent(s)
Expertise
None
Assumed by author(s)
Expertly specified
Tolerance Expression
Residue of Concern
Expert
Decision
Submit
Cancel
I. General info
II. Materials and methods
III. Results
Appendix 1a
Test#
Sex
Number
Dose Route
Dose (nominal)
Dose (measu
Remarks
10A
Female
2
Oral
50.0 mg/kg
48.5 mg/kg
pooled samples of feces, urine, and bil
10B
Female
2
Oral
48.5 mg/kg
pooled samples of feces, urine, and bi
used solely as a source of fecal and ur
Appendix2
Relation
Tree
List
ID
Common Name / Code
Chemical Name
Rat
Click on this icon to bring up the STRUCTURE DRAWING EDITOR – follow directions from previous section in this guidance referring to structural drawing package.
An Appendix 2 Editor window pops up, a chemical name is entered.
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.



Add structure via COPY/PASTE of the SMILES string

Then hit OK

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

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

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

Test#	Sex	Number	Dose Route	Dose (nominal)	Dose (measu	otor	Remarks
10A	Female	2	Oral	50.0 mg/kg	48.5 mg/kg		pooled samples of feces, urine, and bil
10B	Female	2	Oral	50.0 mg/kg	48.5 mg/kg		pooled samples
10C	Female	2	Oral	50.0 mg/kg	48.5 mg/kg		pooled samples
11A	Male	2	Oral	100.0 mg/kg	104.8 mg/kg		used solely as a
11B	Male	2	Oral	100.0 mg/kg	104.8 mg/kg		used solely as a
12A	Female	2	Oral	100.0 mg/kg	110.7 mg/kg		used solely as a
12B	Female	2	Oral	100.0 mg/kg	110.7 mg/kg		used solely as a

Appendix2

Tree List

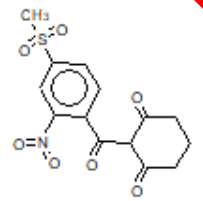
ID	Common Name / Code	Chemical Name	SMILE
1	Mesotrione	Mesotrione (ZA1296)	

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

2:37 PM
2/16/2021

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

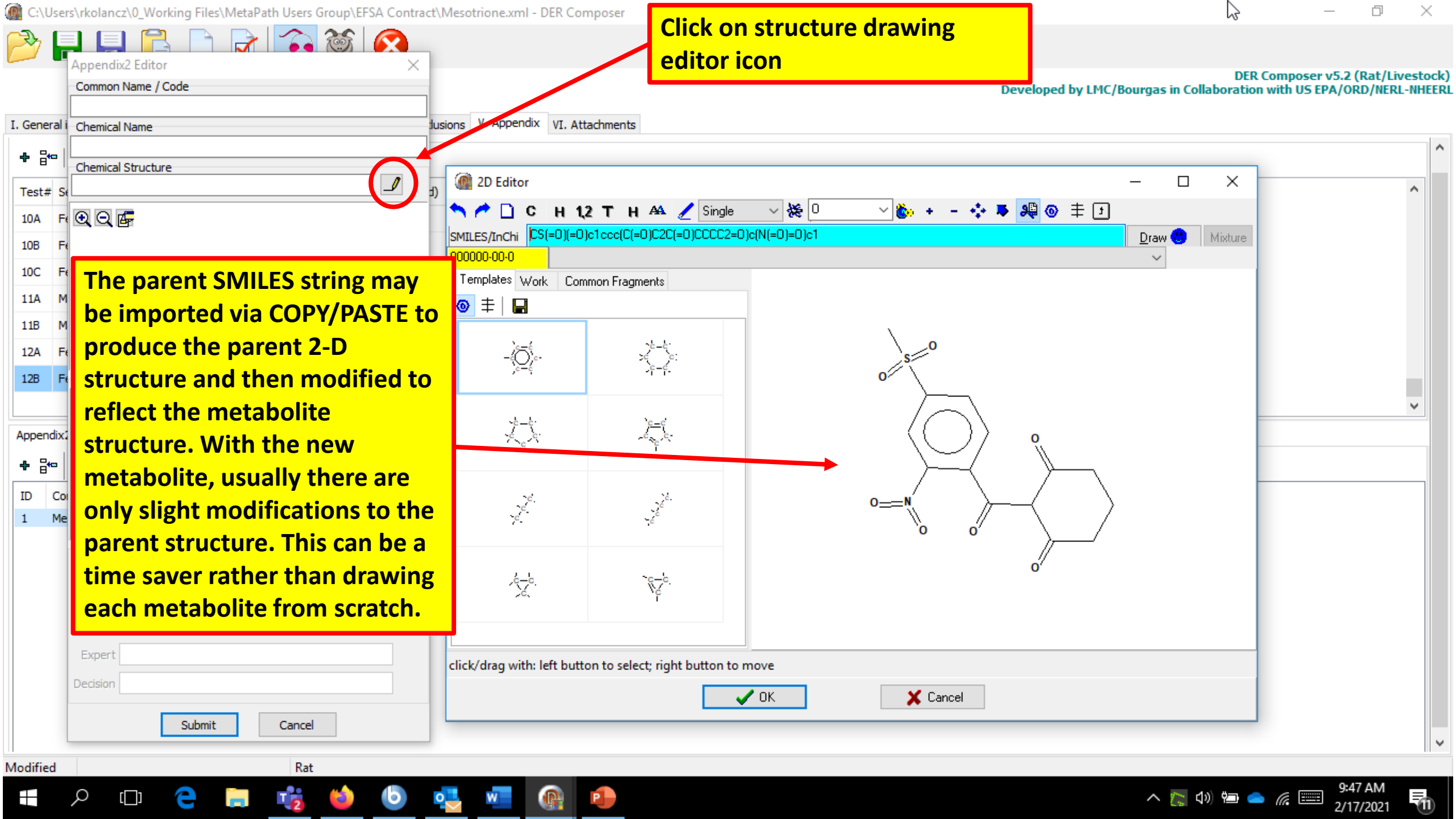
Tree | List

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

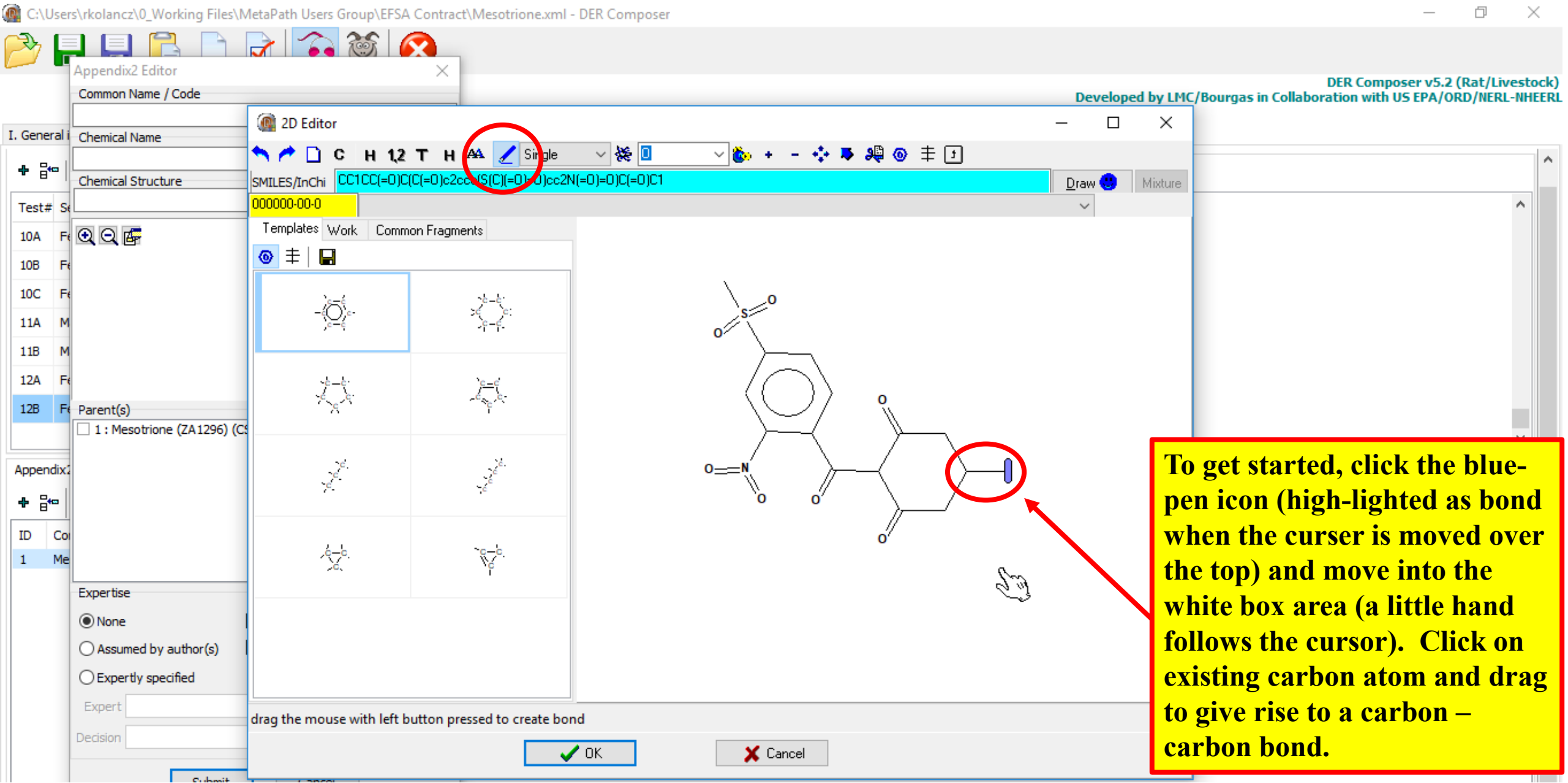
Continue with the next structure (daughter to the parent) by clicking on the + icon once again.

Modified | Rat

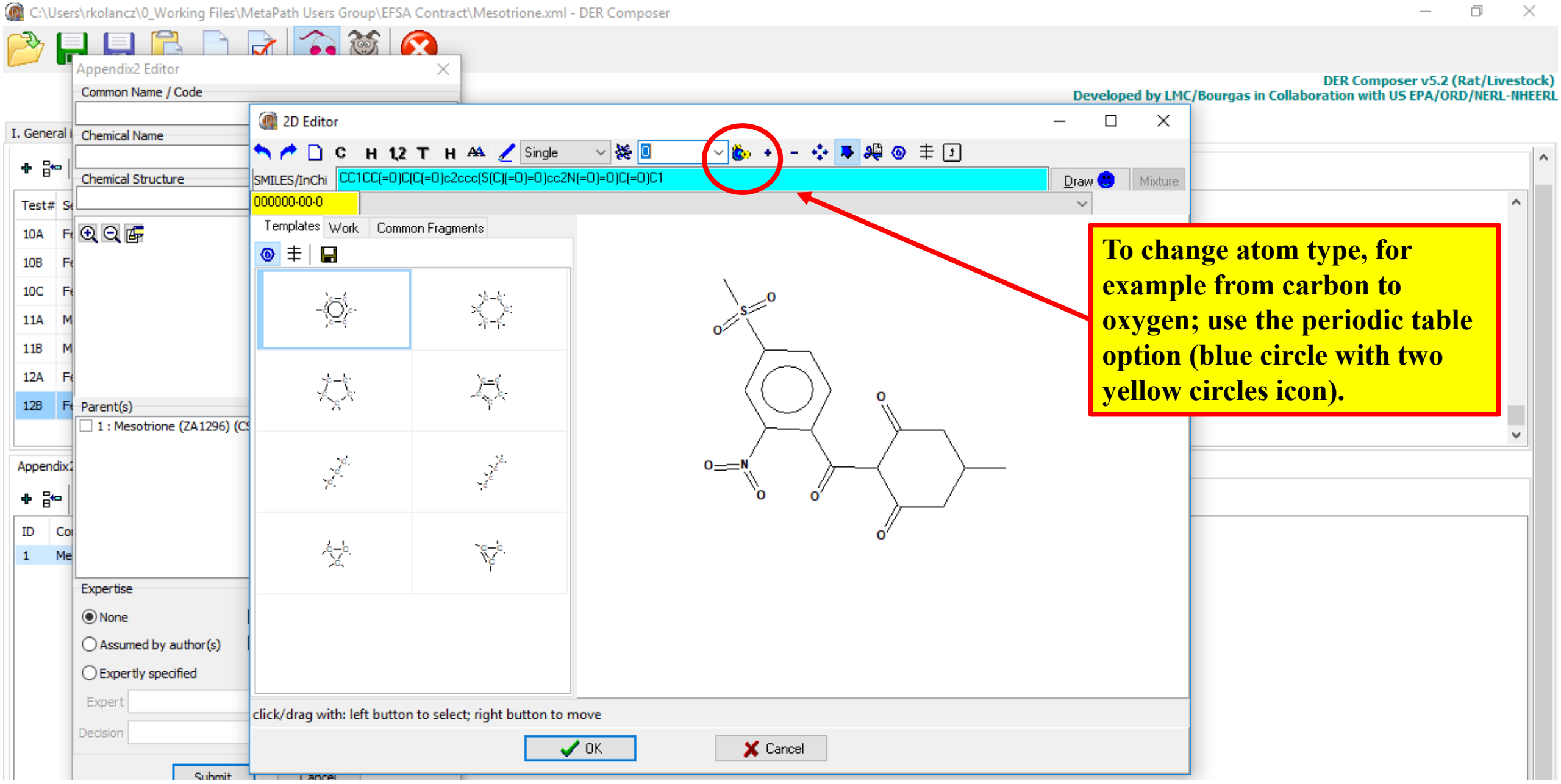
2:40 PM
2/16/2021


Click on structure drawing editor icon
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.
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
Expert
Decision
Submit
Cancel
2D Editor
SMILES/InChi
CS(=O)(=O)c1ccc(C(=O)C2C(=O)CCCC2=O)c(N(=O)=O)c1
Draw
Mixture
Templates
Work
Common Fragments
click/drag with: left button to select; right button to move
OK
Cancel
I. General
V. Appendix
VI. Attachments
Modified
Rat
9:47 AM
2/17/2021

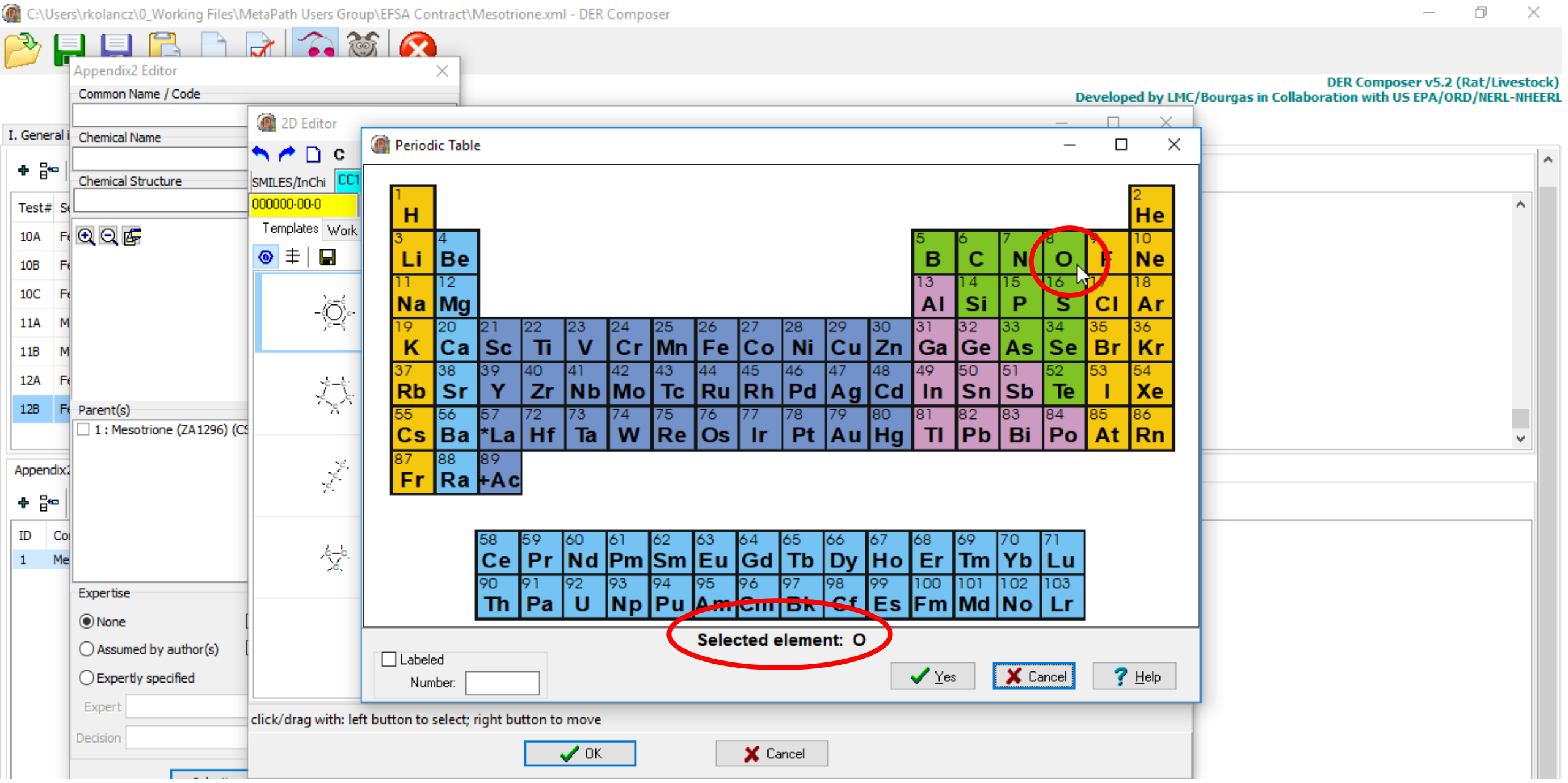
In this example the metabolite is 5-hydroxy-mesotrione. The following steps will introduce a hydroxy group in the 5-position of the dione ring.



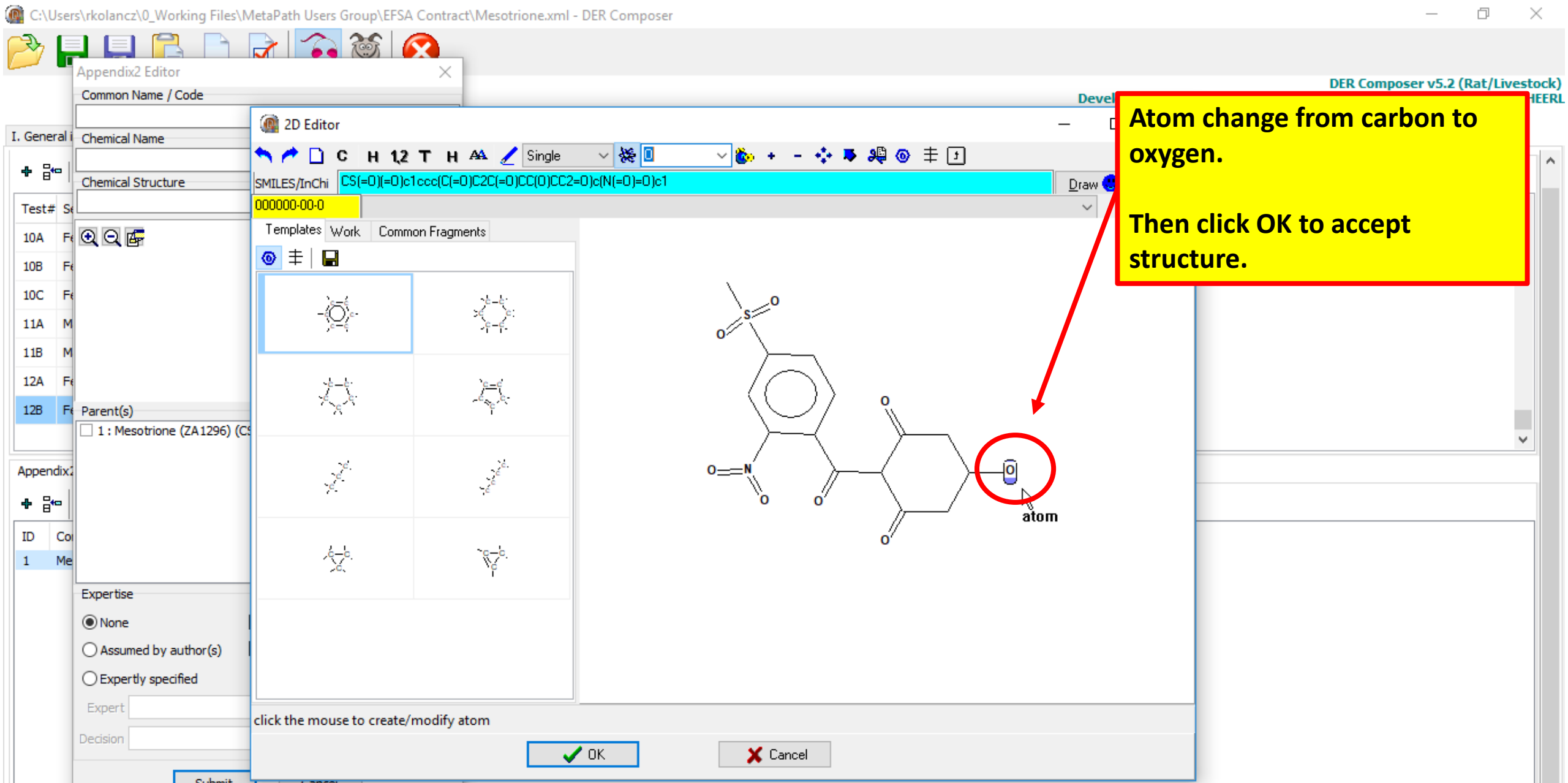
To change atom type, for example from carbon to oxygen; use the periodic table option (blue circle with two yellow circles icon).



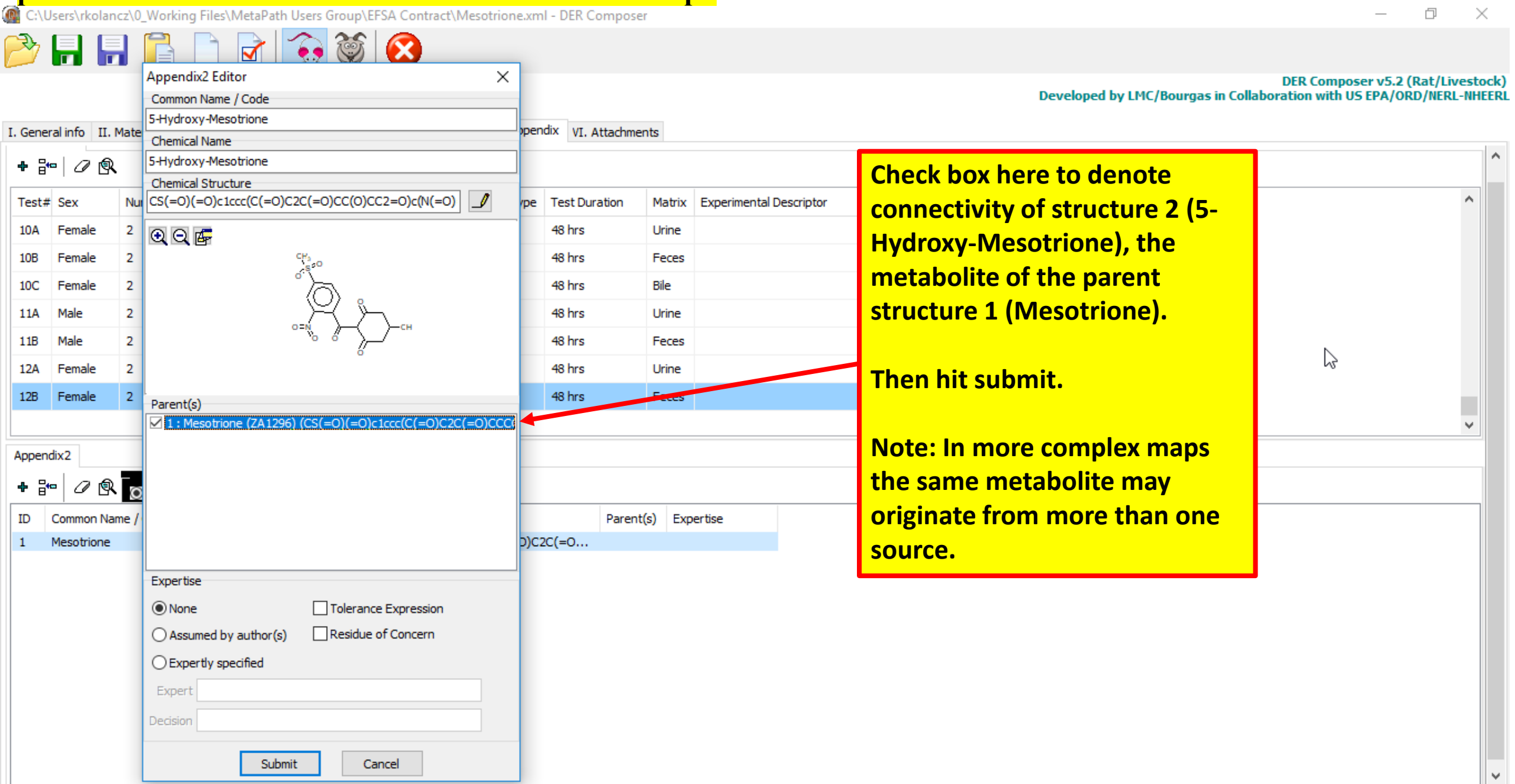
The periodic table opens, click on atom choice, click Yes to accept choice and the table goes away.



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



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.

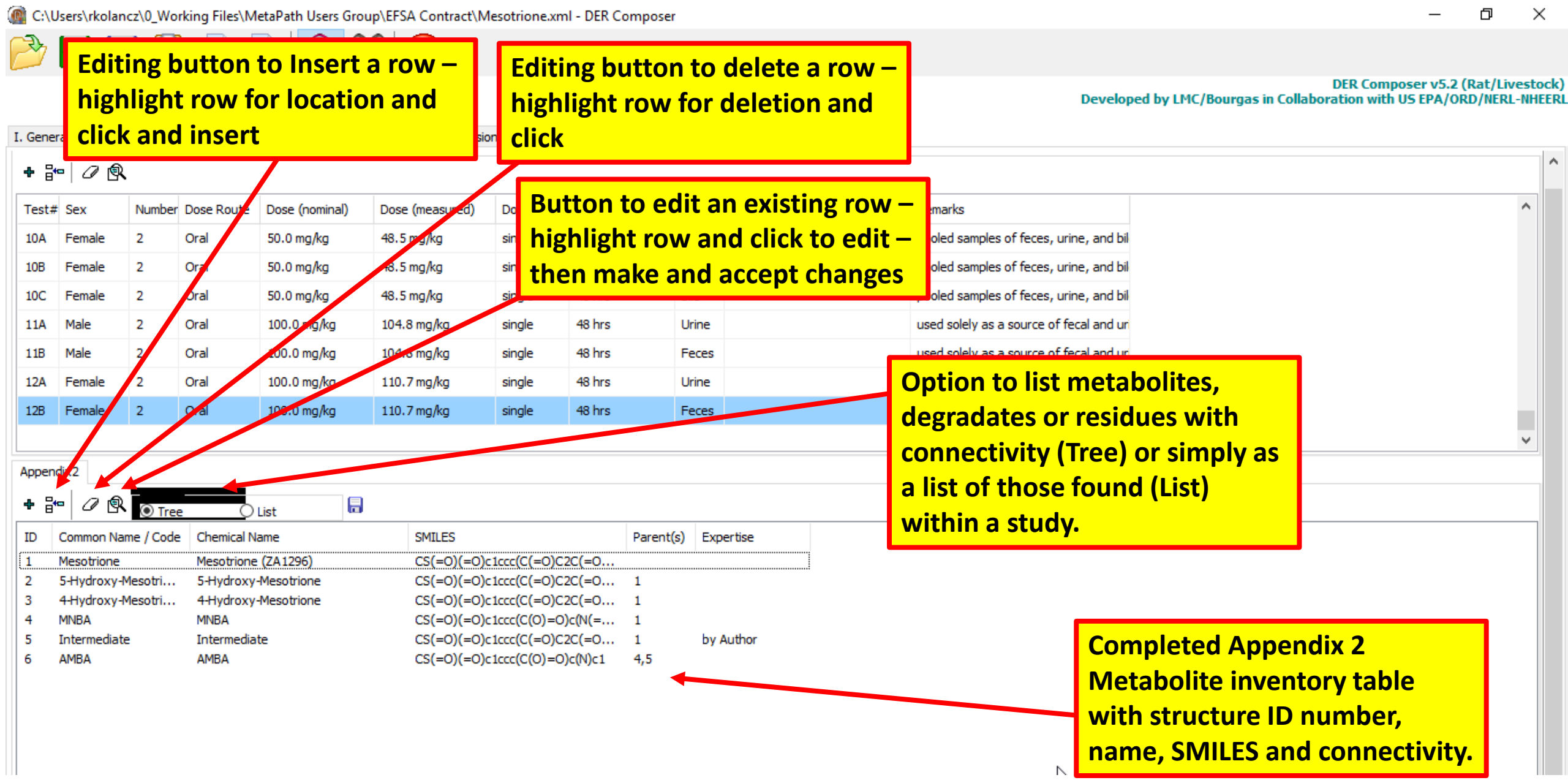


Check box here to denote connectivity of structure 2 (5-Hydroxy-Mesotrione), the metabolite of the parent structure 1 (Mesotrione).

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

DER Composer v5.2 (Rat/Livestock)
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I. General info | II. Mate | ppendix | VI. Attachments

Test#	Sex	Nu	ype	Test Duration	Matrix		
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		used solely as a source of fecal and ur
12B	Female	2		48 hrs	Feces		used solely as a source of fecal and ur

Appendix2

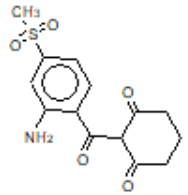
ID	Common Name /	Parent(s)	Expertise
1	Mesotrione		
2	5-Hydroxy-Meso	1	
3	4-Hydroxy-Meso	1	
4	MNBA	1	
5	Intermediate	1	by Author
6	AMBA	4,5	

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)
- [x] 1 : Mesotrione (ZA1296) (CS(=O)(=O)c1ccc(C(=O)C2C(=O)CCC(
- [ ] 2 : 5-Hydroxy-Mesotrione (CS(=O)(=O)c1ccc(C(=O)C2C(=O)CC(
- [ ] 3 : 4-Hydroxy-Mesotrione (CS(=O)(=O)c1ccc(C(=O)C2C(=O)CC(
- [ ] 4 : MNBA (CS(=O)(=O)c1ccc(C(O)=O)c(N(=O)=O)c1)
- [ ] 6 : AMBA (CS(=O)(=O)c1ccc(C(O)=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.

Modified | Rat

11:27 AM
2/17/2021

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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DER Composer v5.2 (Rat/Livestock)
Developed by LMC/Bourgas 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. Materials | B. Study design and methods

1. Group arrangements

Animals were assigned to the test groups noted in Table1

Table1a

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"

Add narrative text throughout within this section.

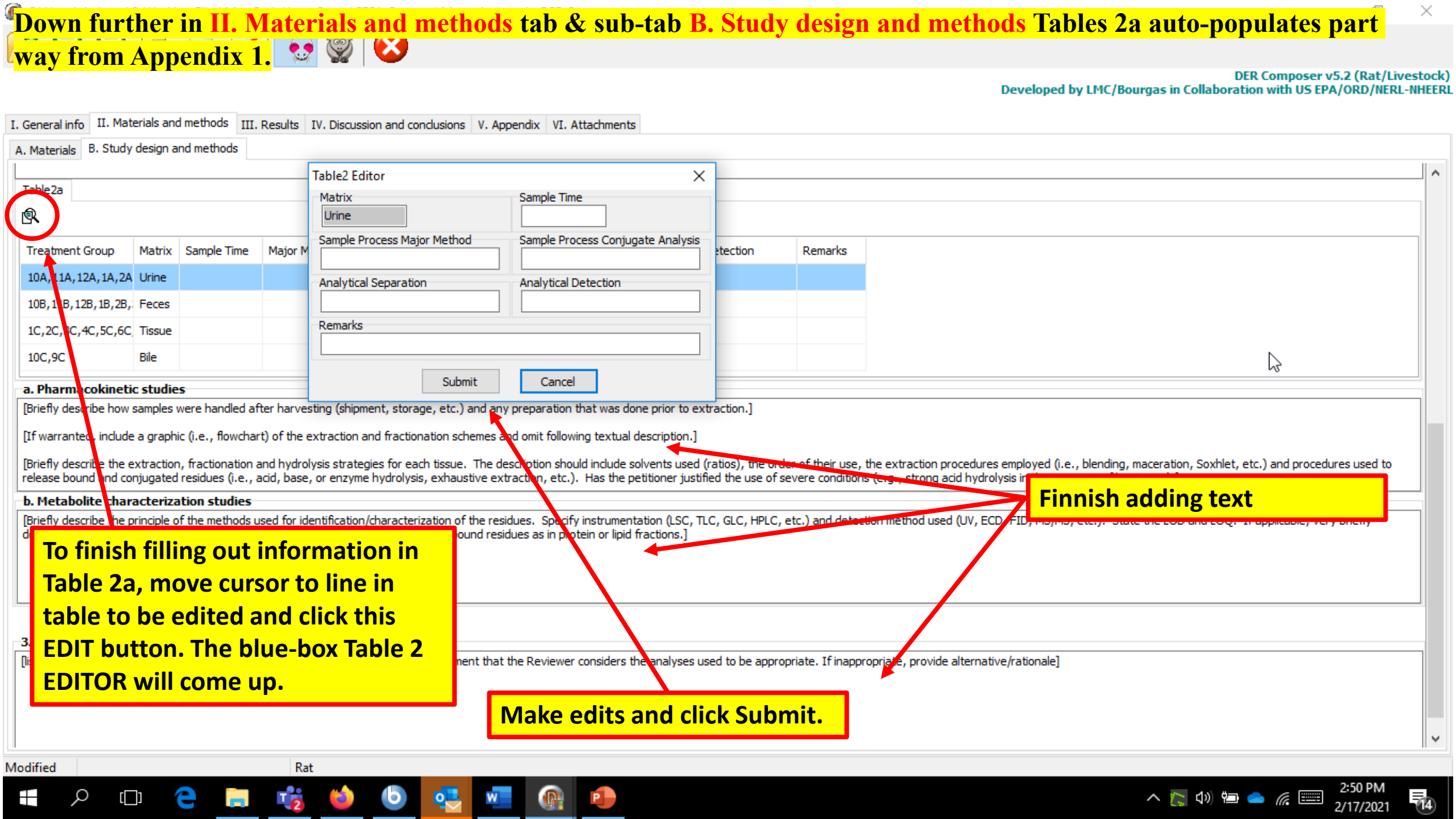
2. Dosing and sample collection

Briefly describe dosing methods and sample collection

Table2a

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

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



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.

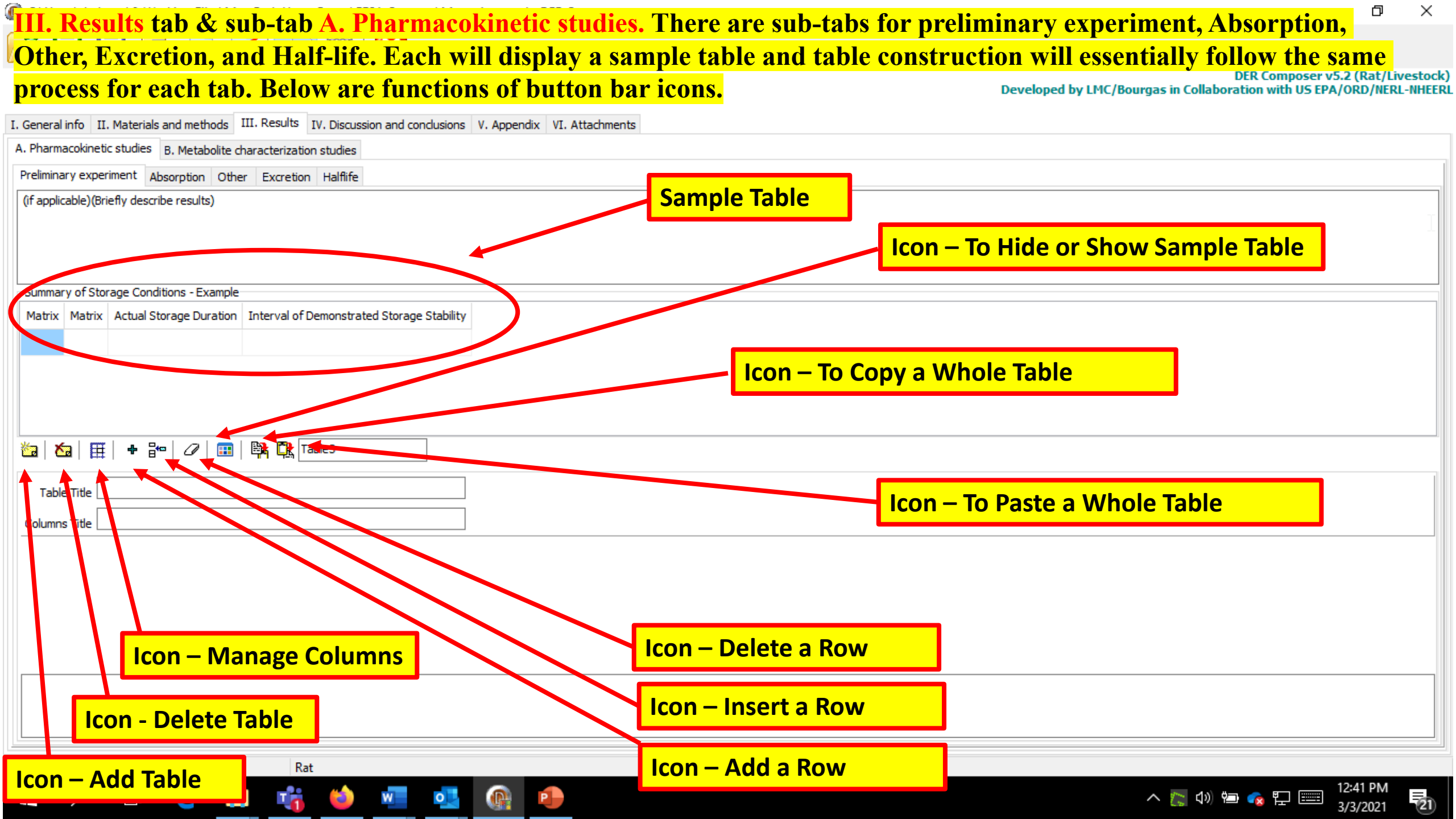
Finnish adding text

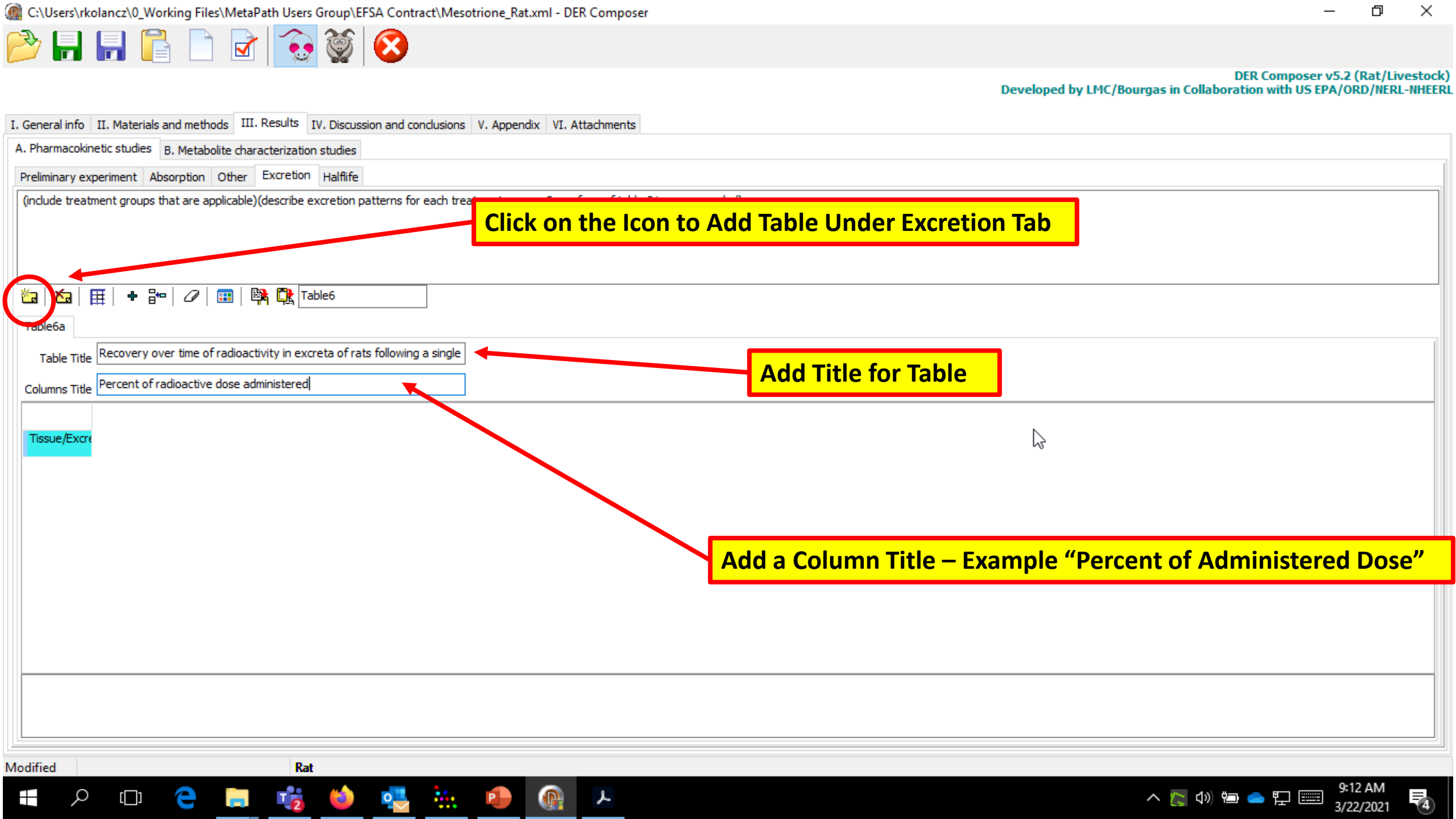
Make edits and click Submit.

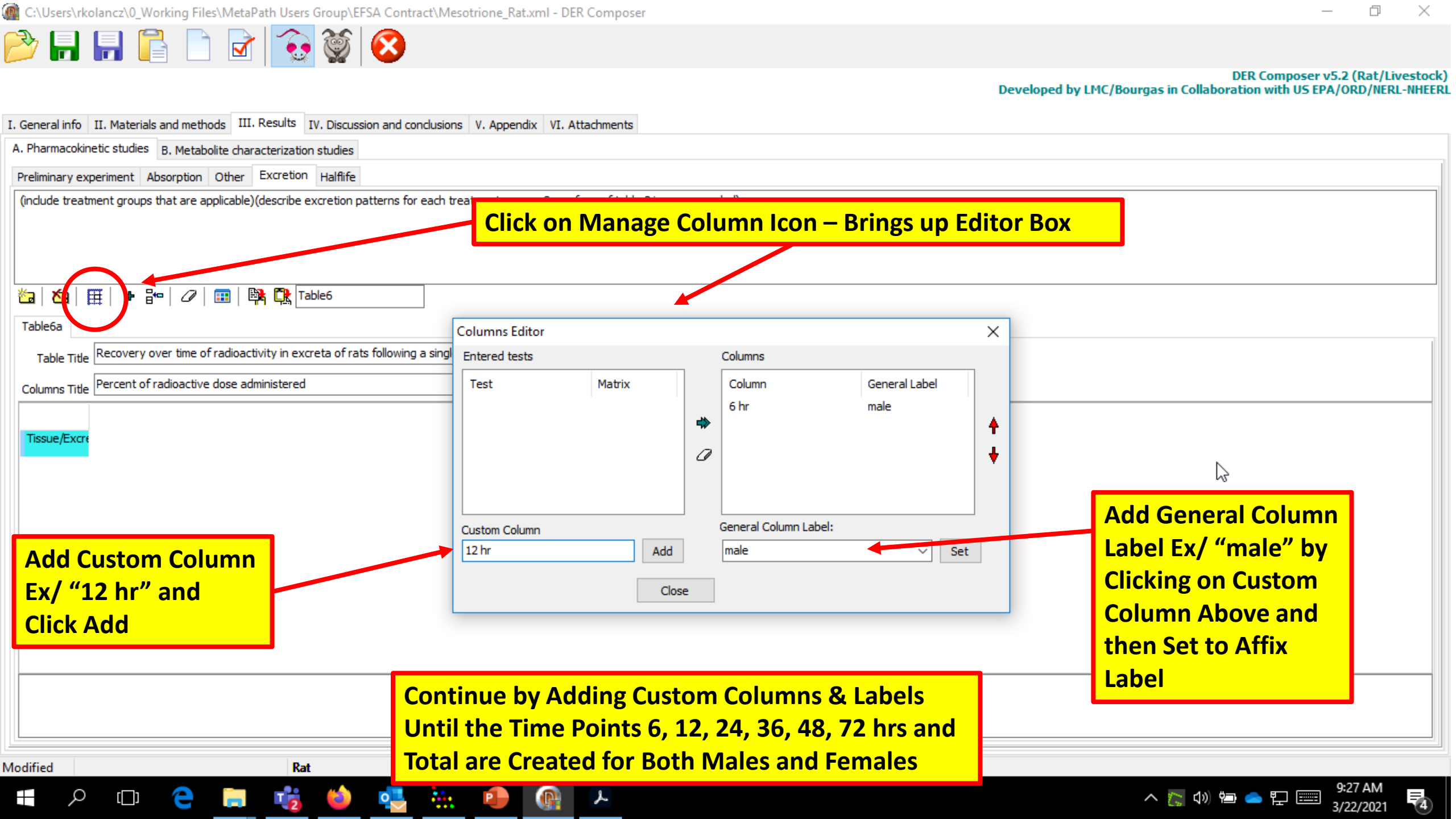
- **Results**

(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.




C:\Users\rkolancz\0_Working Files\MetaPath Users Group\EFSA Contract\Mesotrione_Rat.xml - DER Composer
DER Composer v5.2 (Rat/Livestock)
Developed by LMC/Bourgas 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 trea
Table6
Table6a
Table Title
Recovery over time of radioactivity in excreta of rats following a single
Columns Title
Percent of radioactive dose administered
Tissue/Excre
Click on the Icon to Add Table Under Excretion Tab
Add Title for Table
Add a Column Title – Example "Percent of Administered Dose"
Modified
Rat
9:12 AM
3/22/2021


C:\Users\rkolancz\0_Working Files\MetaPath Users Group\EFSA Contract\Mesotrione_Rat.xml - DER Composer
DER Composer v5.2 (Rat/Livestock)
Developed by LMC/Bourgas in Collaboration with US EPA/ORD/NERL-NHEERL
I. General info
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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 trea
Table6
Table6a
Table Title
Recovery over time of radioactivity in excreta of rats following a singl
Columns Title
Percent of radioactive dose administered
Tissue/Excre
Click on Manage Column Icon – Brings up Editor Box
Columns Editor
Entered tests
Test
Matrix
Columns
Column
General Label
6 hr
male
Custom Column
12 hr
Add
General Column Label:
male
Set
Close
Add Custom Column Ex/ “12 hr” and Click Add
Add General Column Label Ex/ “male” by Clicking on Custom Column Above and then Set to Affix Label
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
9:27 AM
3/22/2021

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

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

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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 treatm

Click Close When Done with Editor

Table6

Table6a

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

Columns Title: Percent of radioactive dose administered

Tissue/Excre

Columns Editor

Entered tests

Test	Matrix

Columns

Column	General Label
24 hr	female
36 hr	female
48 hr	female
72 hr	female
Total	female

Custom Column: Add

General Column Label: female — Set

Close

Modified | Rat

9:49 AM
3/22/2021

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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

(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

10:16 AM
3/22/2021

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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

(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

10:44 AM
3/22/2021

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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

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 e cretion. In the single female kept to 48 hours, 9verall 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 singlei

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

Modified | Rat

3:04 PM
3/22/2021

- **Results**

(Metabolite characterization studies)

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DER Composer v5.2 (Rat/Livestock)
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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

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 cannuiated 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.

Modified | Rat

3:07 PM
3/22/2021

Metabolic Pathways - application ver.5.3.0.8, database ver.3.3.0 - RegulatoryDB_771_June 2020_v3.3.0.MTB, logged in as "administrator"

File Edit Search View Options Help

Developed by LMC Bourgas in collaboration with US EPA / ORD / NER

RegulatoryDB_771_June 2020_v3.3.0.MTB | PFAS Open Lit_Aug2020_v3.3.0.MTB

Locked by: administrator

Regulatory ID quick search

ID

Value

Select

1. 220899-03-6; Metrafenone [Br
2. 220899-03-6; Metrafenone [Tr
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 ri
10. 335104-84-2; Tembotrione [1
11. 335104-84-2; Tembotrione [1
12. 420-04-2; Cyanamide [C14];

IUPAC name	Metrafenone; (3-bromo-6-me
PC code	000325
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

Redraw | Print Preview | Map font

CAS:220899-03-6; Metrafenone [Bromophenyl-6-
Rat, in vivo (x8)
1) Mallipudi, N.M. (2002) BAS 560F (AC 375839): absorption, distribution, metabolism, and excretion study in the rat. BASF Corp
Laboratory Project Identification: 98025, April 30, 2002. MR

boro, NJ.

Metrafenone (BAS 560F)

CL 3000402 | CL 376991 | CL 434223 | CL 377160 | 1Xinterm to CL1500700

CIT

CL 1023427 | CL 1500701 | CL 1500699 | CL 377096 | CL 1500698 | CL 1500700

CL 1500702 | CL 1500697

Metabolic Pathways - Highlight treatment groups

Common fields:

Rat; in vivo; oral; 10 mg/kg; nominal _measured dose; radiolabeled parent; single dose; Sprague-Dawley (Crl: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

Collapse | Hide details

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

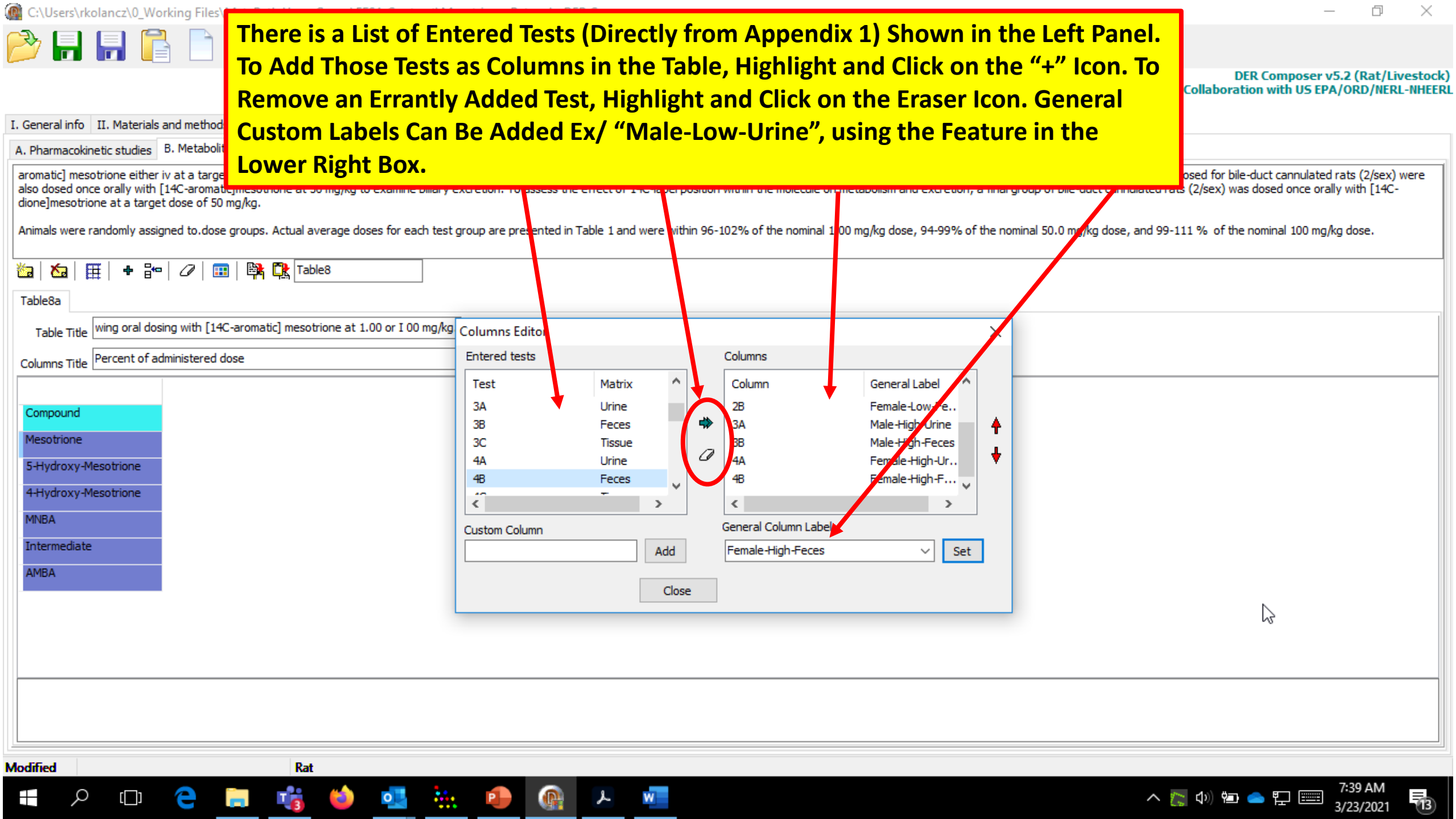
Citations:
Mallipudi, N.M. (2002) BAS 560F (AC 375839): absorption, distribution, metabolism, and excretion study in the rat. BASF Corporation, BASF Agro Research, Princeton, NJ, and XenoBiotic Laboratories, Inc., Plainsboro, NJ. Laboratory Project Identification: 98025, April 30, 2002. MRID 46415747.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

Subjects:
- *Species* - Rat
- *Gender* - Female (5 subjects)
- *Weight* - Between 150 - 350 grams (female)
- *Age* - Between 6 - 10 weeks old
- *Strain* - Sprague-Dawley (Crl: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

Enviromental 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

1:29 PM
3/22/2021


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. Metaboli
aromatic] mesotrione either iv at a targe
osed 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 I 00 mg/kg
Columns Title
Percent of administered dose
Compound
Mesotrione
5-Hydroxy-Mesotrione
4-Hydroxy-Mesotrione
MNBA
Intermediate
AMBA
Columns Editor
Entered tests
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
Add
General Column Label
Female-High-Feces
Set
Close
Modified
Rat
7:39 AM
3/23/2021

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

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

I. General info | II. Materials and methods | III. Results | IV. Discussion and conclusions | V. Appen

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 ar ... 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								
5-Hydroxy-Mesotrione								
4-Hydroxy-Mesotrione								
MNBA								
Intermediate								
AMBA								

Add Table Title

Add Column Title

Columns Resulting from the Editor. Basic Structure of Table.

Modified | Rat

7:42 AM
3/23/2021

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

DER Composer v5.2 (Rat/Livestock)
Developed by LMC/Bourgas 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

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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

8:08 AM
3/23/2021

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

DER Composer v5.2 (Rat/Livestock)
Developed by LMC/Bourgas 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

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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

Table8

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….

Modified | Rat

12:49 PM
3/23/2021

- **Conclusions**

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

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

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

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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) th_at 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 [illegible] beled 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 t[illegible]excretion, a final group of bile-duct cannuiated rats (2/sex) was dosed once orally with [14C-dione]mesotrione at a target dose of 50 mg/kg.

Use These Icons to Add or Insert a New Row

Table8

Table8a

Table Title: 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
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

1:18 PM
3/23/2021

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

DER Composer v5.2 (Rat/Livestock)
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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-Fe				Female-High-Feces
Compound	1A	1B	2A	2B	[illegible]	[illegible]	[illegible]	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

Save or Save As the XML

Might be a good idea to do frequent saves of your work during the data capture process.

Modified | Rat

1:24 PM
3/23/2021

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

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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-Fe...				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

Generate the WORD Document.

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

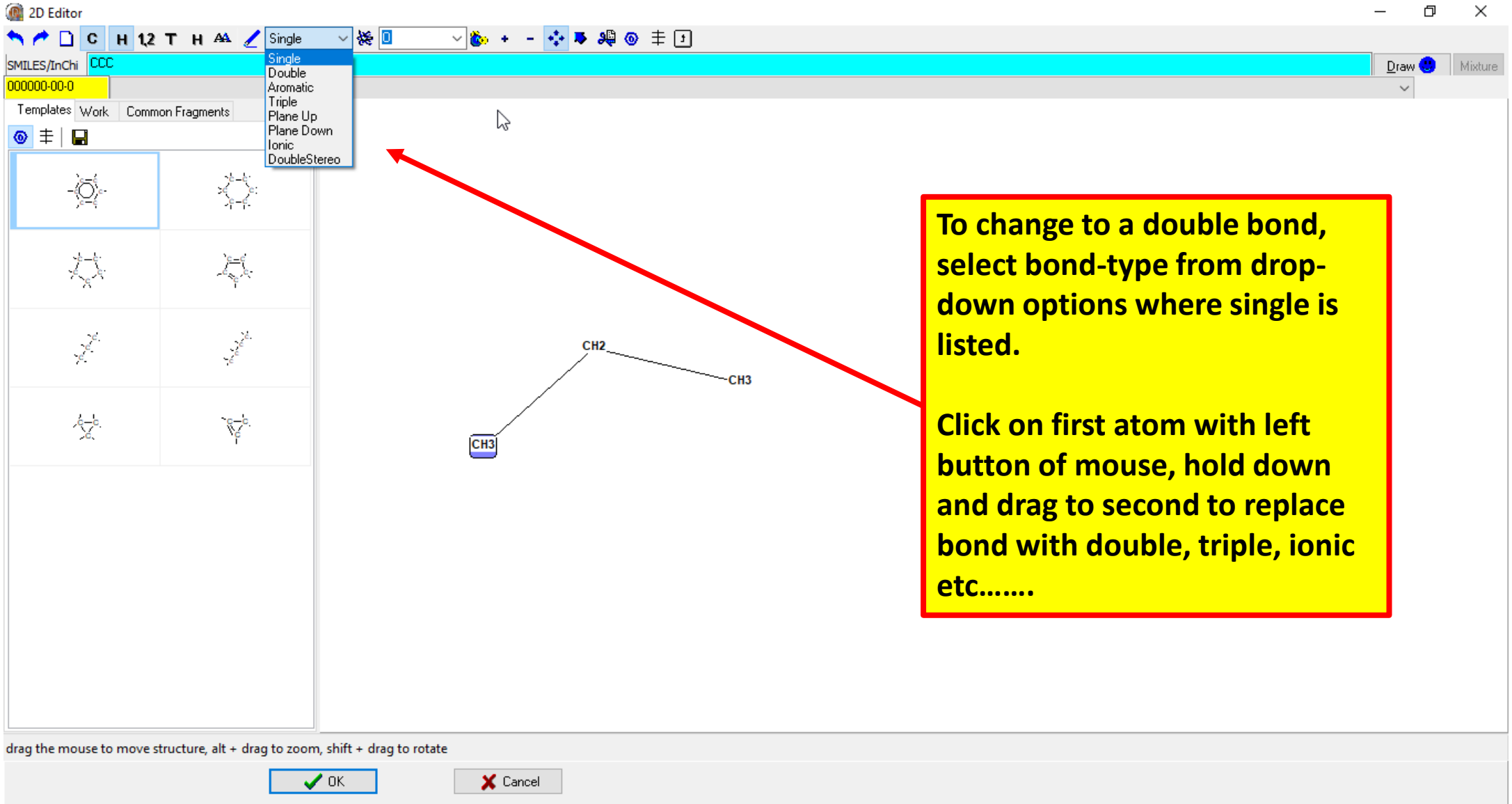
Modified | Rat

1:24 PM
3/23/2021

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

STRUCTURE EDITING

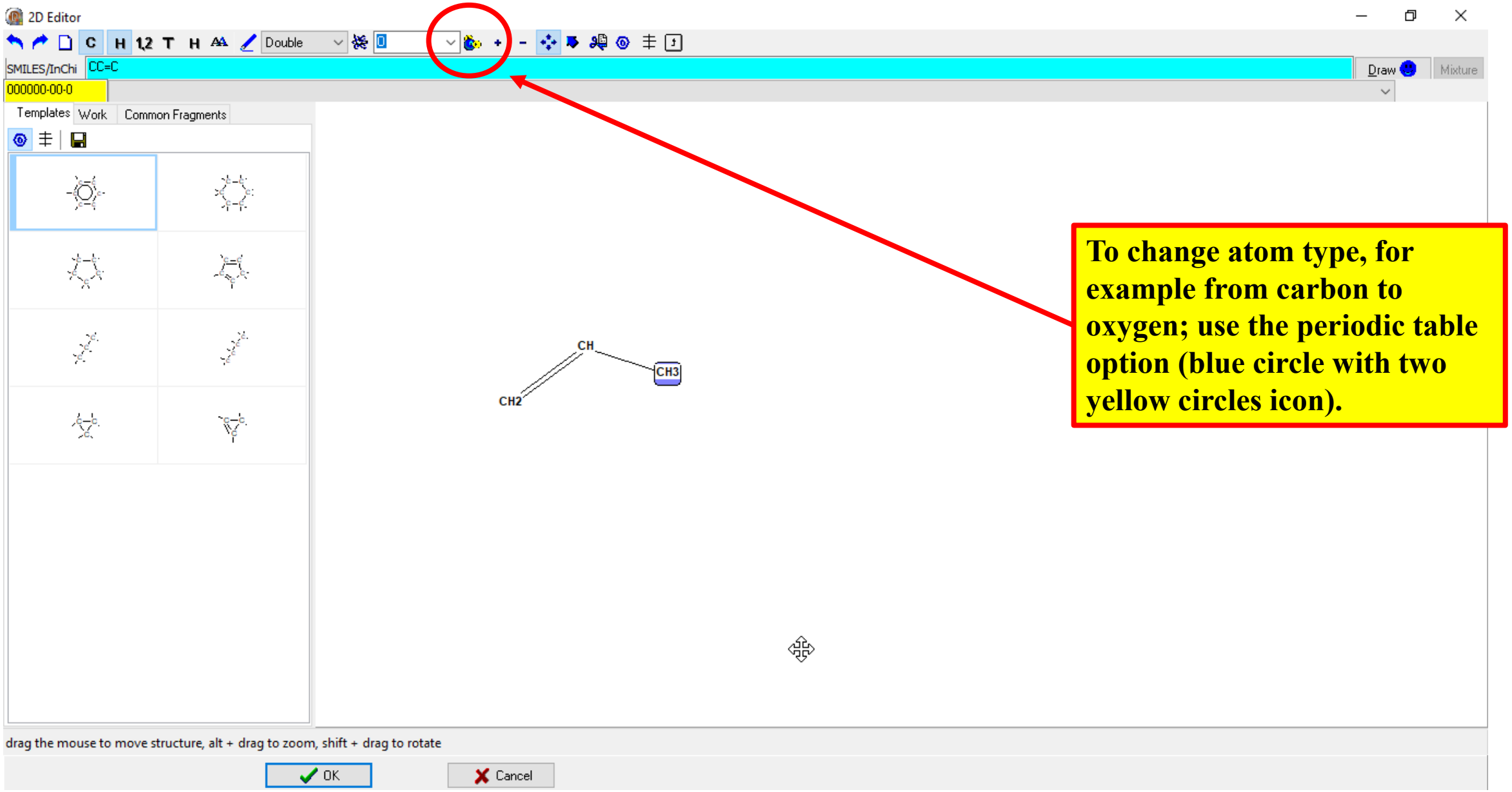
The following screen-shots illustrate some other functions of the STRUCTURE DRAWING package that may be used to modify/edit/draw 2-D structures of parent/metabolites.



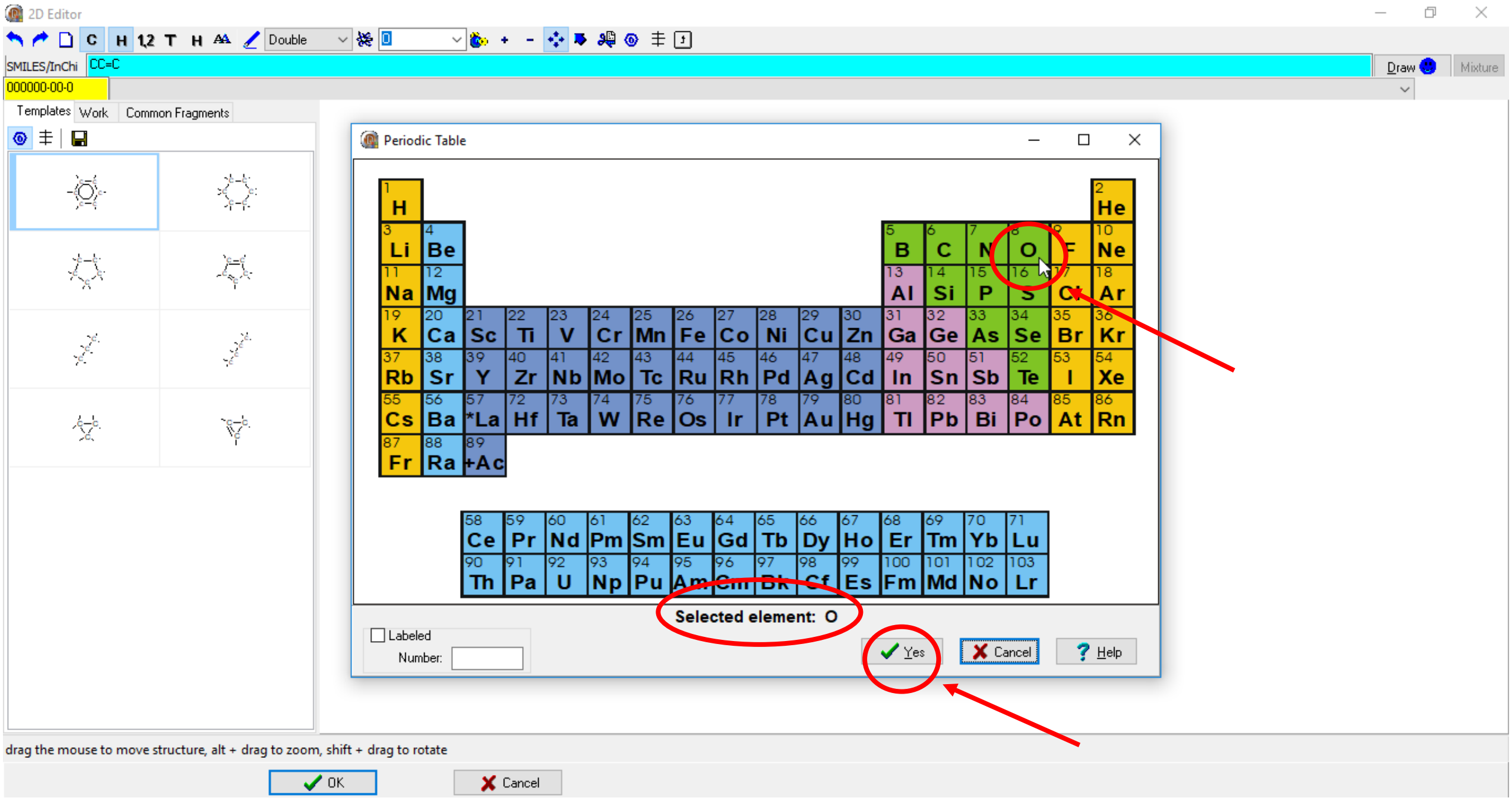
To change to a double bond, select bond-type from drop-down options where single is listed.

Click on first atom with left button of mouse, hold down and drag to second to replace bond with double, triple, ionic etc…….

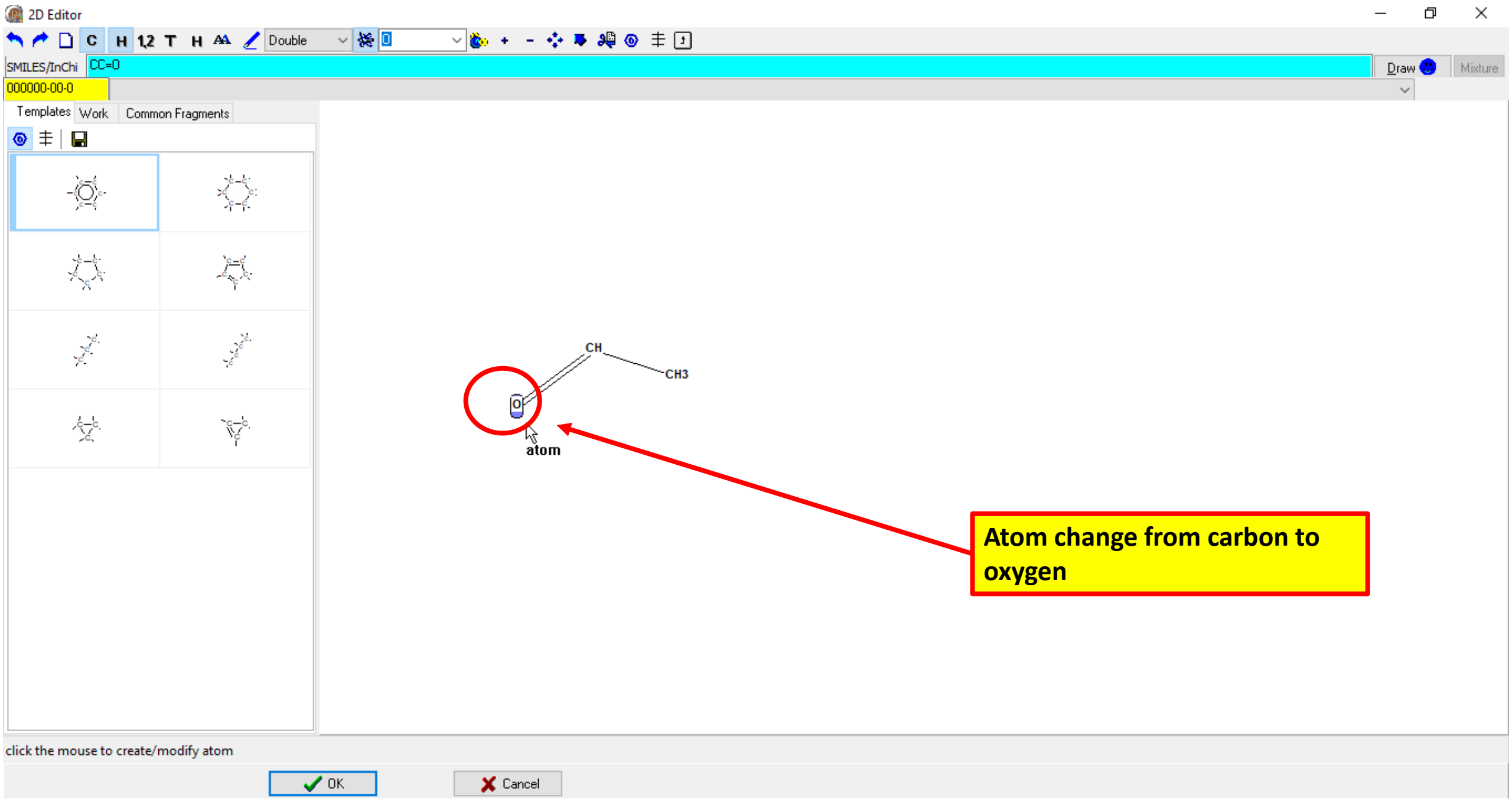
To change atom type, for example from carbon to oxygen; use the periodic table option (blue circle with two yellow circles icon).

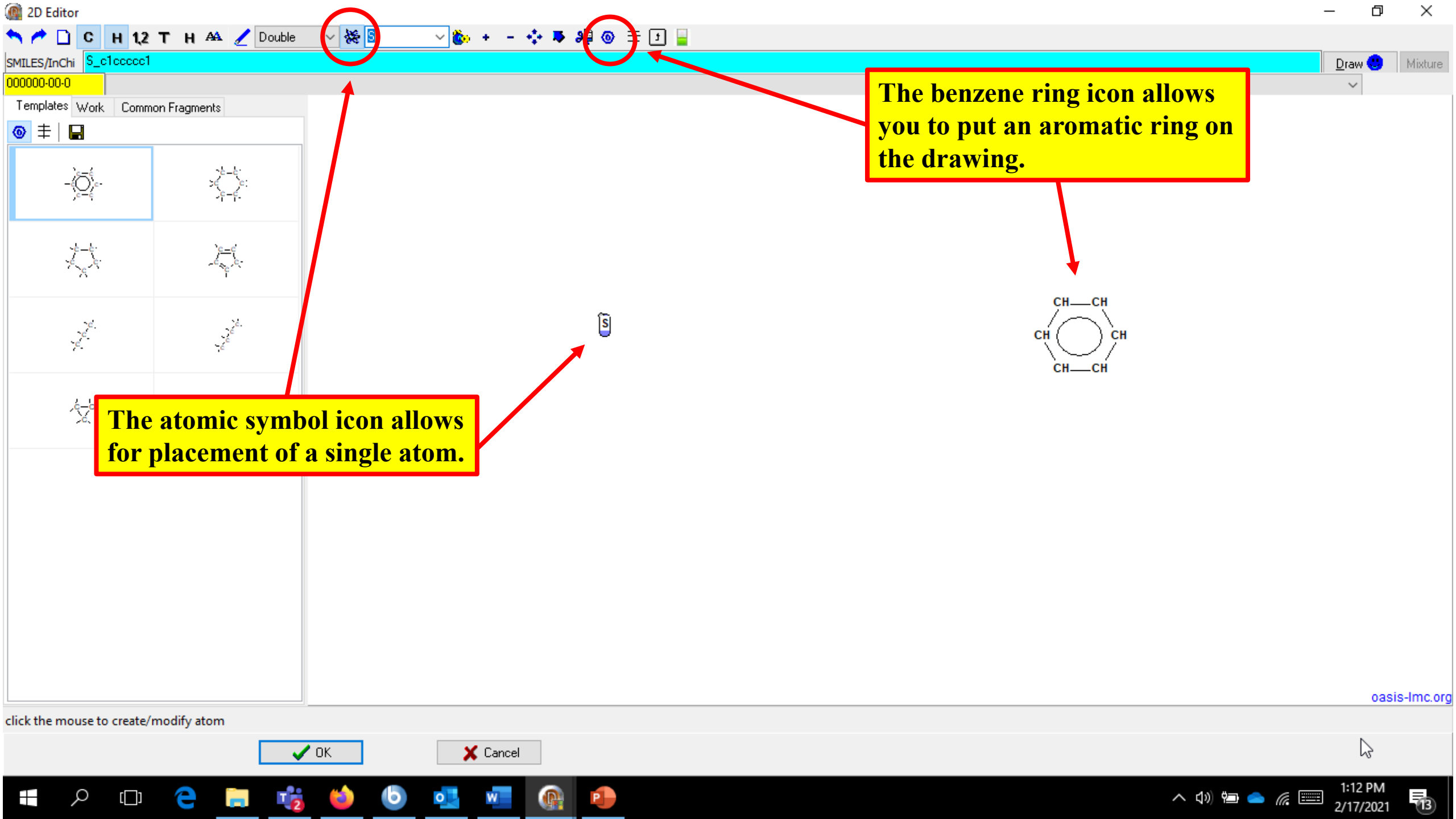


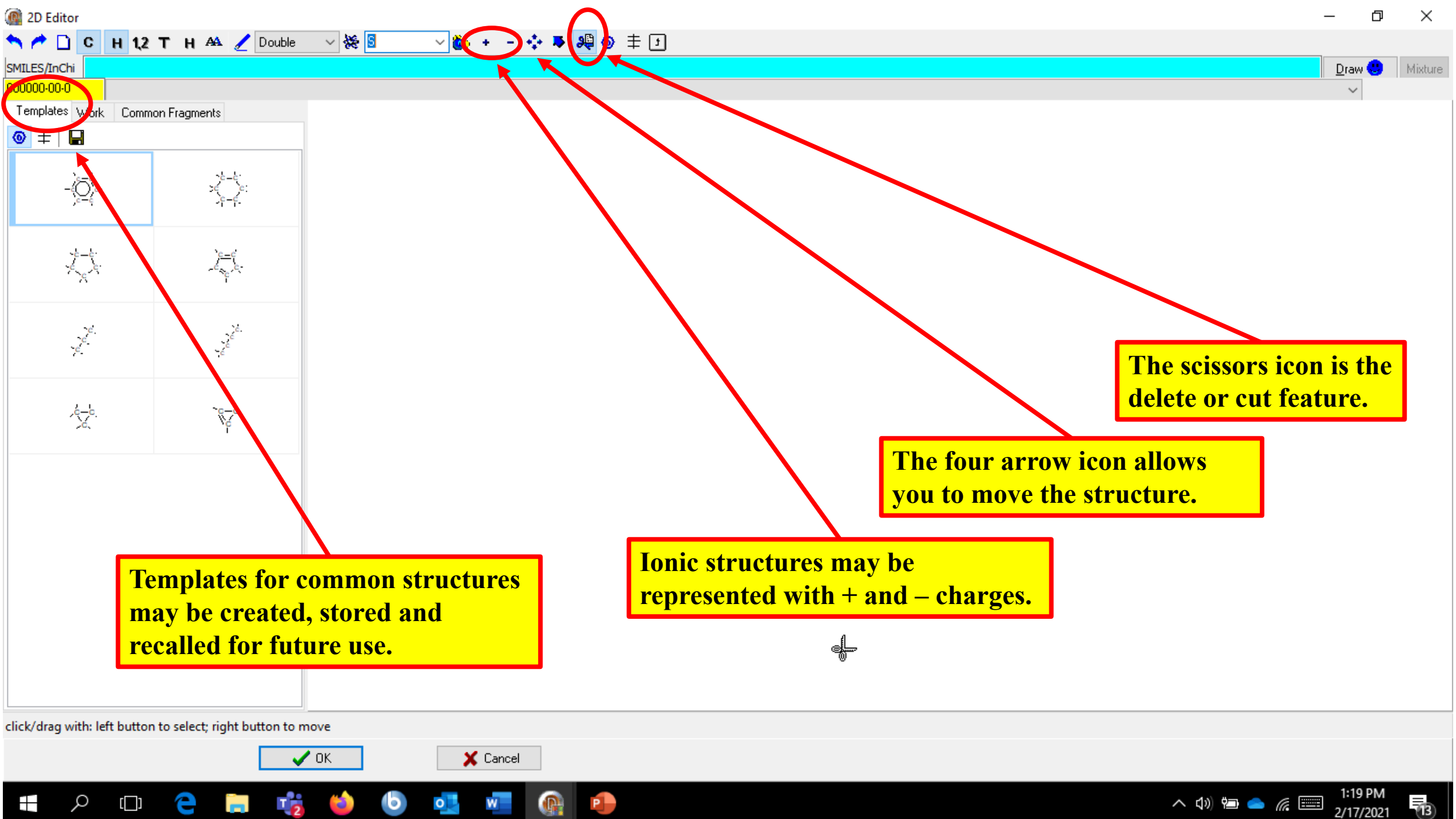
The table opens, click on atom choice, click yes to accept choice and the table goes away.



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




2D Editor
Double
SMILES/InChi
S_c1ccccc1
Draw
Mixture
000000-00-0
Templates
Work
Common Fragments
The benzene ring icon allows you to put an aromatic ring on the drawing.
CH—CH
CH
CH
CH—CH
The atomic symbol icon allows for placement of a single atom.
oasis-lmc.org
click the mouse to create/modify atom
OK
Cancel
1:12 PM
2/17/2021


2D Editor
Double
SMILES/InChi
Draw
Mixture
000000-00-0
Templates
Work
Common Fragments
Templates for common structures may be created, stored and recalled for future use.
Ionic structures may be represented with + and – charges.
The four arrow icon allows you to move the structure.
The scissors icon is the delete or cut feature.
click/drag with: left button to select; right button to move
OK
Cancel
1:19 PM
2/17/2021

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