

OncoLogic™

Quick Start Tutorial

A Step-by-Step Guide to
Using OncoLogic™ to Predict Potential
Carcinogenicity

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1. OncoLogic™ - How it works

- Designed to mimic the thinking and reasoning of human experts
- Uses knowledge-based rules for chemical classes to predict cancer concern
- Evaluates how substituents on the chemical may affect carcinogenicity – Concern level changes accordingly
- Assigns a baseline concern level ranging from low to high

1.1. Concern Level

OncoLogic™ Concern	Definition
Low	Unlikely to be carcinogenic.
Marginal	Likely to have equivocal carcinogenic activity.
Low-Moderate	Likely to be weakly carcinogenic.
Moderate	Likely to be a moderately active carcinogen.
Moderate-High	Highly likely to be a moderately active carcinogen.
High	Highly likely to be a potent carcinogen.

1.2. Two Separate Methods

1.2.1. SAR Analysis

- OncoLogic™ uses mechanism-based SAR analysis to predict potential carcinogenicity
- Analysis is based upon knowledge of the structural and biological bases of carcinogenicity of various classes of chemical carcinogens
- Incorporates knowledge-based rules and chemical-specific user input
- Rules were developed jointly by cancer experts and system development experts based on cancer studies and scientific publications

1.2.2. Functional Analysis

- Integrates the results of available mechanistic / non cancer studies on the chemical to predict potential carcinogenicity
 - Study results are entered by the user
 - If no such studies are available, only SAR Analysis can be performed
- Must be performed independently of SAR Analysis
- Can be used to provide support to the results of structural analysis, or can be used as an independent method of analysis of carcinogenicity

2. Starting OncoLogic™

OncoLogic™ can be started with any of the following two ways

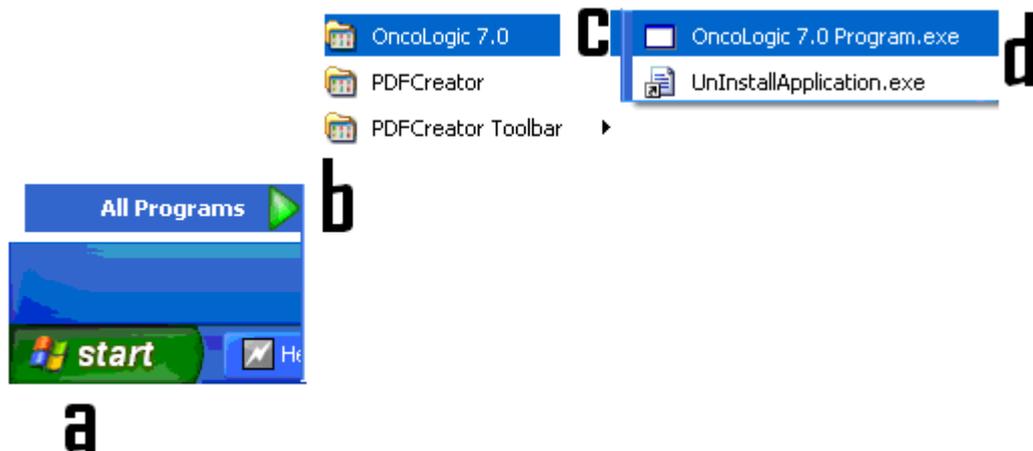
1. The OncoLogic Set-Up (Installation) Program places a “Desktop Icon” on the Windows Desktop similar to the Icon shown here:



If desired, this Icon is easily removed from the Windows Desktop by “dragging” it to the Recycle Bin or by placing the mouse pointer on the Icon, right-mouse button clicking, and then deleting.

2. To run OncoLogic with other option follow steps mentioned below

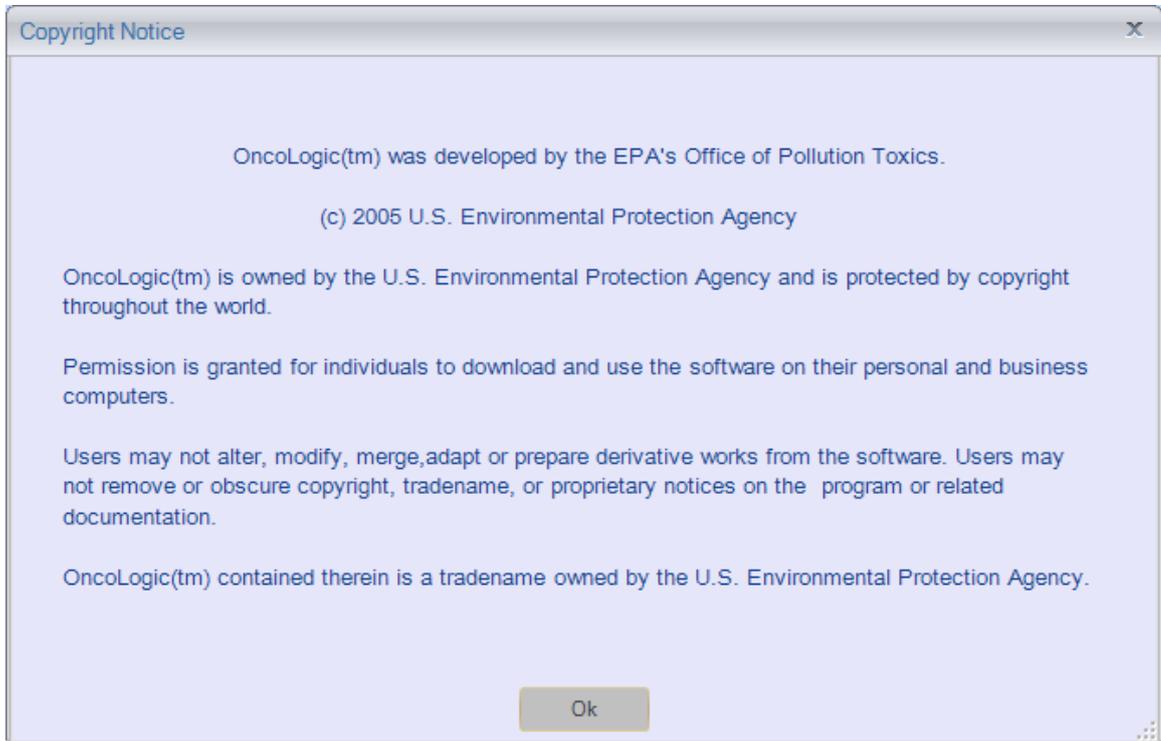
- a. Press the “Start” Button
- b. Select “All Programs”
- c. Select “OncoLogic 7.0”
- d. Select “OncoLogic 7.0.exe”



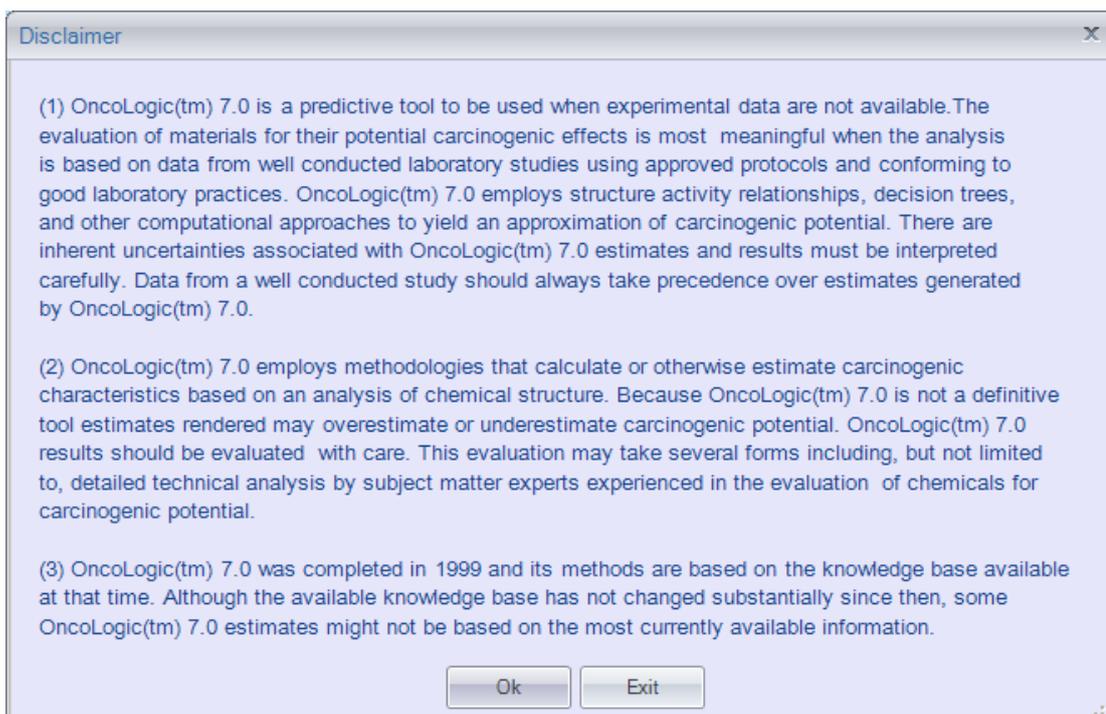
3. Running OncoLogic

When you start OncoLogic application you will get the Disclaimer screen

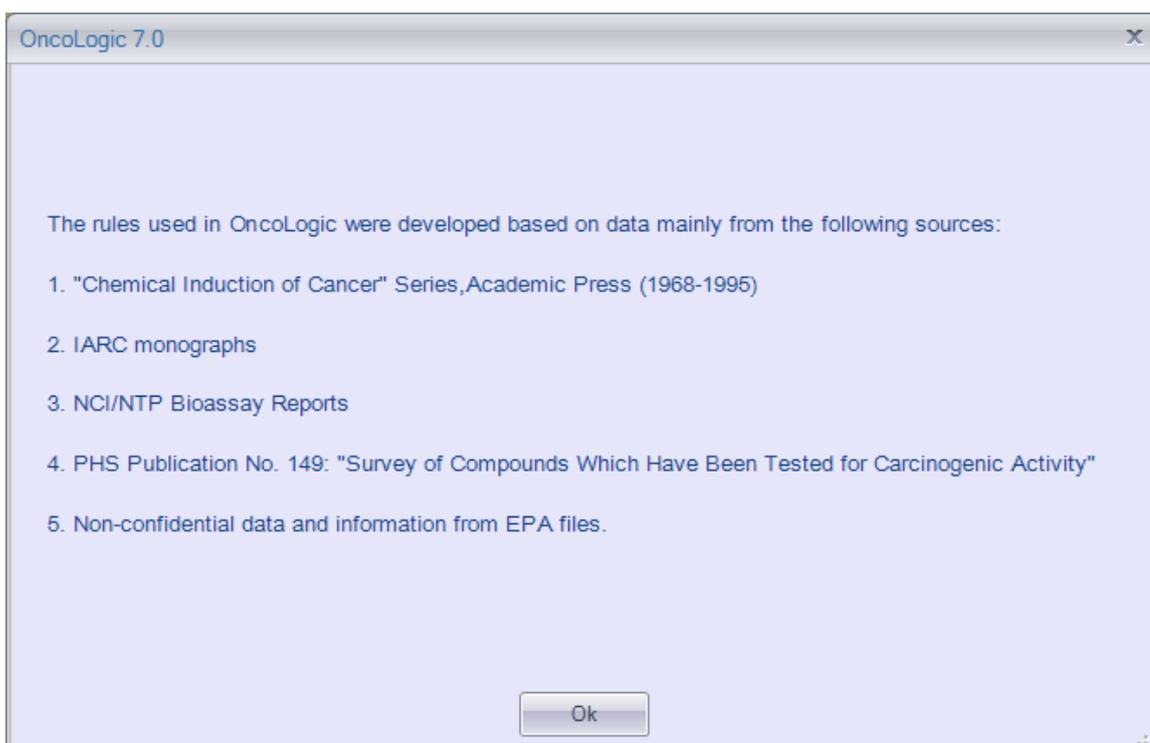
Click “Ok” at the Copyright screen to acknowledge that you accept the terms and conditions of using OncoLogic™.



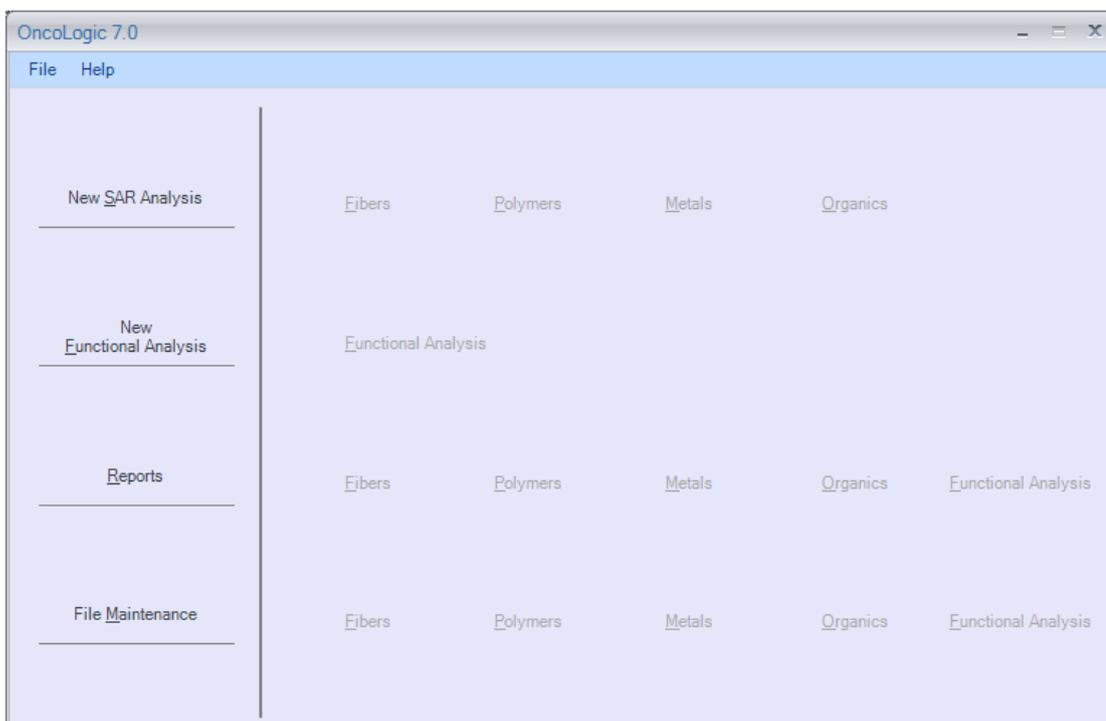
Click “Ok” at the Disclaimer screen



Click “Ok” at the screen that describes the development of OncoLogic™ rules



Select from one of the four options displayed, which are briefly described on the next screen.

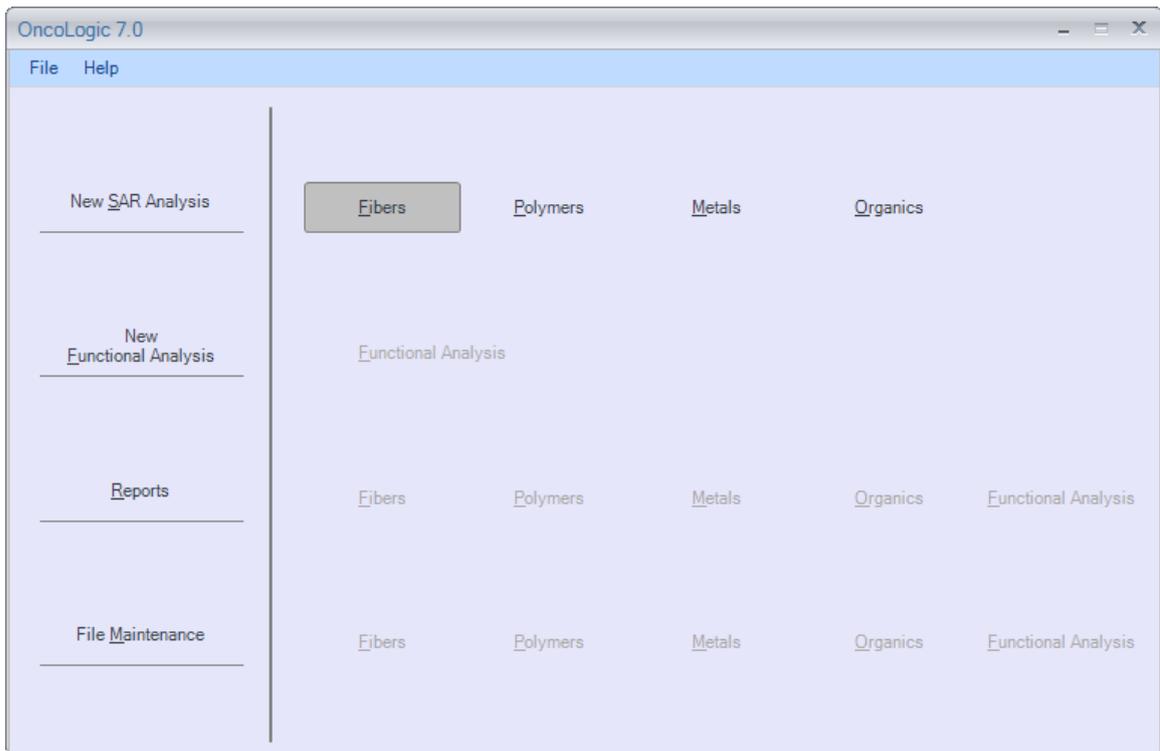


This screen shows following option

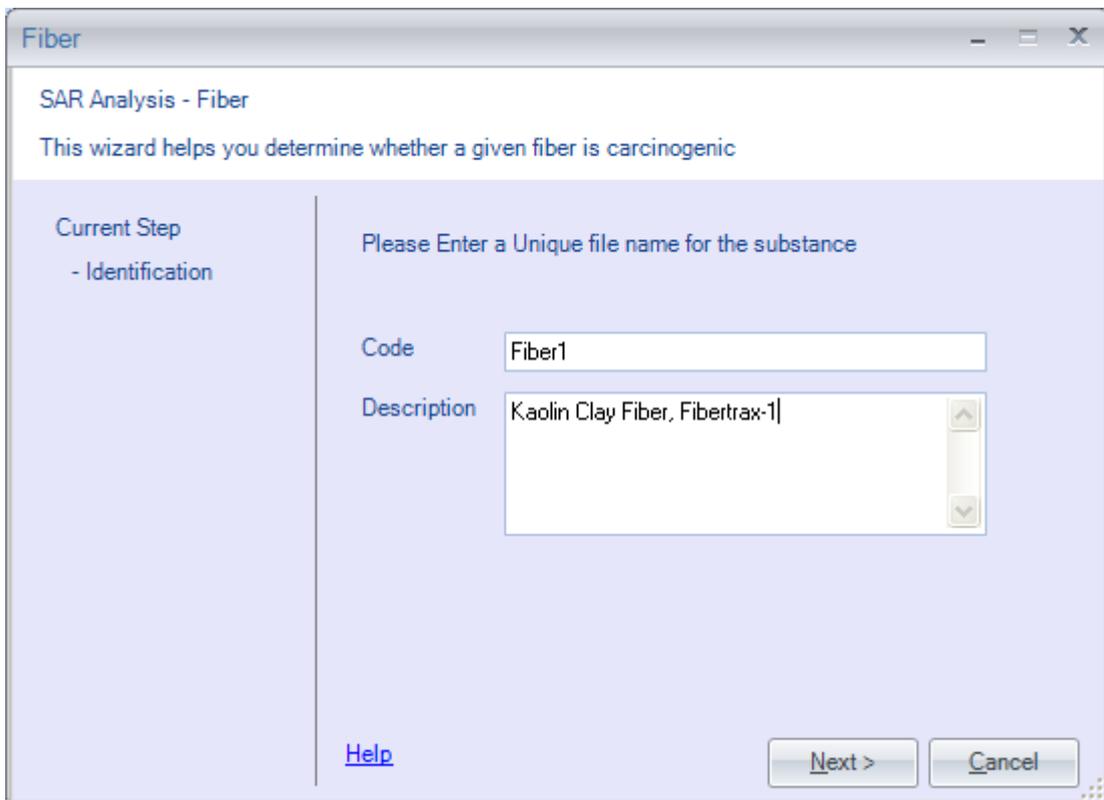
- **SAR Analysis** : Uses knowledge rules to predict carcinogenicity
 - Four Modules
 - Fibers
 - Polymers
 - Metals
 - Organics
- **Functional Analysis** : Uses mechanistic / non-cancer studies to predict carcinogenicity
- **Reports** : View or print OncoLogic™ reports and user input data
- **File Maintenance** : Delete or Copy reports

3.1. Running Fiber Module

- Evaluations are based on physical dimensions and physicochemical properties
- Questions may request information on
 - Physical dimensions like
 - Diameter, length, aspect ratio
 - Physicochemical properties like
 - High density charge, flexibility, durability, biodegradability, smooth and defect-free surface, longitudinal splitting potential, Presence of high MW polymer, low MW organic moiety, metals/metalloids



Select Fibers.



Enter code: Fiber1.

Enter Description: Kaolin Clay Fiber, Fibertrax 1

If a filename was used before, you will be asked to enter a different filename.

You may change what you have typed by using the <Backspace> key.

Press: <Next> when you are ready to continue.

You may enter any type of character for the substance identification. There is a limit of 240 letters, numbers, etc. that may be entered. Any more than 240 characters will not be accepted.

The screenshot shows a window titled "Fiber" with a subtitle "SAR Analysis - Fiber". Below the subtitle is the text "This wizard helps you determine whether a given fiber is carcinogenic". The window is divided into two main sections. On the left, a vertical sidebar indicates the "Current Step" as "- Water Solubility". The main area on the right contains the question "Does the substance swell, coalesce, or dissolve in water ?" followed by three radio button options: "Yes", "No", and "Unknown". The "No" option is selected. At the bottom of the window, there is a blue "Help" link, and three buttons: "< Back", "Next >", and "Cancel".

Select: No, and press "Next"

The screenshot shows the same "Fiber" window, now at the second step. The sidebar indicates the "Current Step" as "- Diameter". The main area contains the text "The diameter of the substance, if known, can be given as a single value or the range of values. Please select the appropriate option." followed by three radio button options: "Single Value", "Range Of Values", and "Unknown". The "Single Value" option is selected. Below the options is the instruction "Please enter the diameter of the substance in microns" and a text input field containing the value "0.22". At the bottom, there is a blue "Help" link and three buttons: "< Back", "Next >", and "Cancel".

Select: Single Value

Enter 0.22 and press <Next>.

The screenshot shows a window titled "Fiber" with a subtitle "SAR Analysis - Fiber". Below the subtitle is the text "This wizard helps you determine whether a given fiber is carcinogenic". On the left side, under "Current Step", it says "- Length". The main area contains the instruction: "The length of the substance, if known, can be given as a single value or the range of values. Please select the appropriate option." There are three radio button options: "Single Value" (which is selected), "Range Of Values", and "Unknown". Below these is the text "Please enter the length of the substance in microns" and a text input field containing the number "5.5". At the bottom, there is a "Help" link and three buttons: "< Back", "Next >", and "Cancel".

Select: Single Value
Enter 5.5 and press <Next>.

The screenshot shows the same "Fiber" window, now at a different step. The "Current Step" is "- Surface Density". The main question is "Does the fiber have a high charge density on its surface?". There are three radio button options: "Yes", "No", and "Unknown" (which is selected). At the bottom, there is a "Help" link and three buttons: "< Back", "Next >", and "Cancel".

Since the given does not specify a charge density, **select** Unknown. , and press “Next”

Fiber

SAR Analysis - Fiber

This wizard helps you determine whether a given fiber is carcinogenic

Current Step
- Production

Please select the method of production of the fiber.

Crystallization
 Naturally Occurring
 Thermal Extrusion
 Unknown

[Help](#)

< Back Next > Cancel

Select: Thermal Extrusion, and press “Next”

Fiber

SAR Analysis - Fiber

This wizard helps you determine whether a given fiber is carcinogenic

Current Step
- Additional Property

Does the fiber exhibit at least one of the following properties?

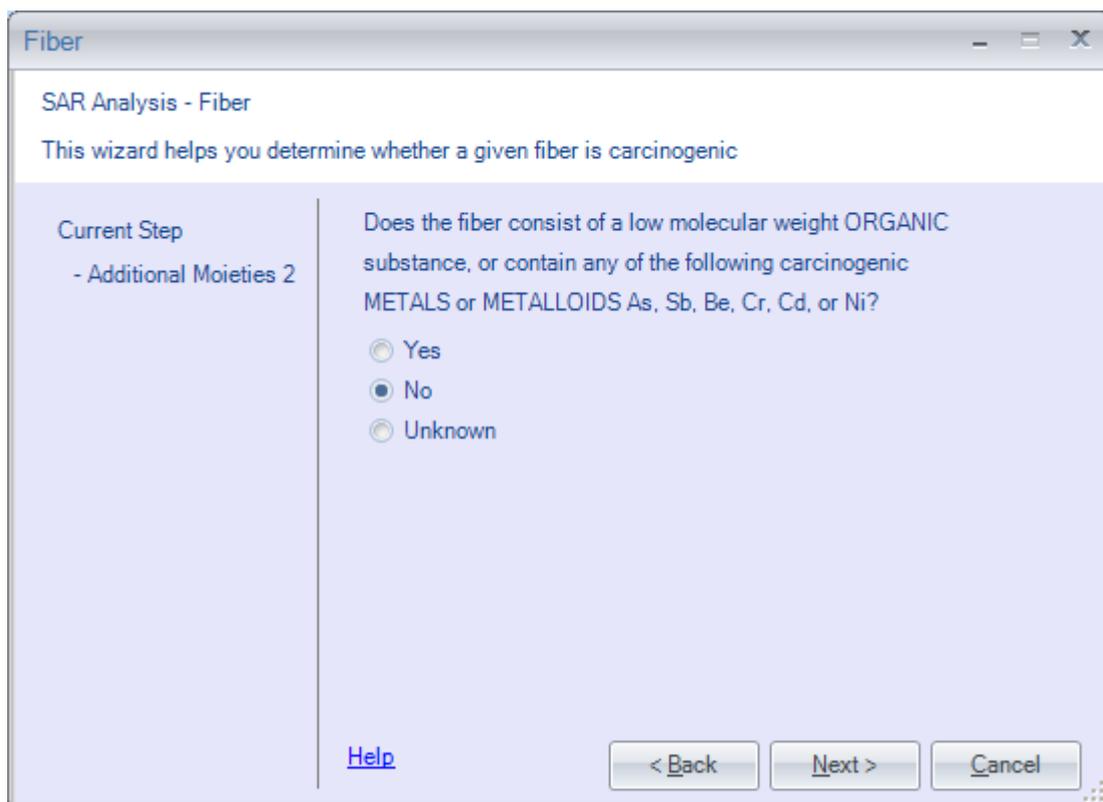
1) Flexibility.
2) High durability.
3) Low or no IN VIVO biodegradability.
4) Smooth, defect-free surface structure.
5) Longitudinal splitting potential.

Yes
 No
 Unknown

[Help](#)

< Back Next > Cancel

Select Yes, and press “Next”



Select No, and press “Next”

At this point, the evaluation will be complete, and the justification report displayed. Because the justification report is more than one page long, you will need to scroll down to read the entire report.

Justification Report

OncoLogic Justification Report

SUMMARY :

Filename : Fiber1

Substance ID : Kaolin Clay Fiber, Fibertrax-1

Diameter Used : 0.22 microns

Length Used : 5.5 microns

Aspect Ratio : 25 microns

The level of concern for carcinogenic potential of this fiber is MODERATE.

JUSTIFICATION

The unifying concept of fiber carcinogenesis is the Stanton Hypothesis. This hypothesis states that the dimensions of a fiber are the major criteria for establishing the concern for its carcinogenic potential.

Since the diameter of the fiber is less than 0.25 microns, its length is less than or equal to 8 microns, and its aspect ratio is greater than 5, the initial level of concern for carcinogenic potential of this fiber is MODERATE.

Fibers that are produced by extrusion, especially thermal/melting treatment, are assumed to have low charge density on their surface since these conditions do not allow time for orderly build-up of surface structure. This decreases the level of concern to LOW-MODERATE.

Justification Report

The fiber exhibits one or more of the following properties: 1) Flexibility 2) Durability 3) Low or no IN VIVO biodegradability (Note: There is insufficient evidence the IN VITRO biodegradability is a valid indicator for IN VIVO biodegradability.) 4) Smooth, defect-free surface 5) Longitudinal splitting potential These characteristics make minor modifications to the concern level and many are inter-related. Thus, regardless of the number of these characteristics the fiber exhibits, the level of concern is increased by only one step to MODERATE.

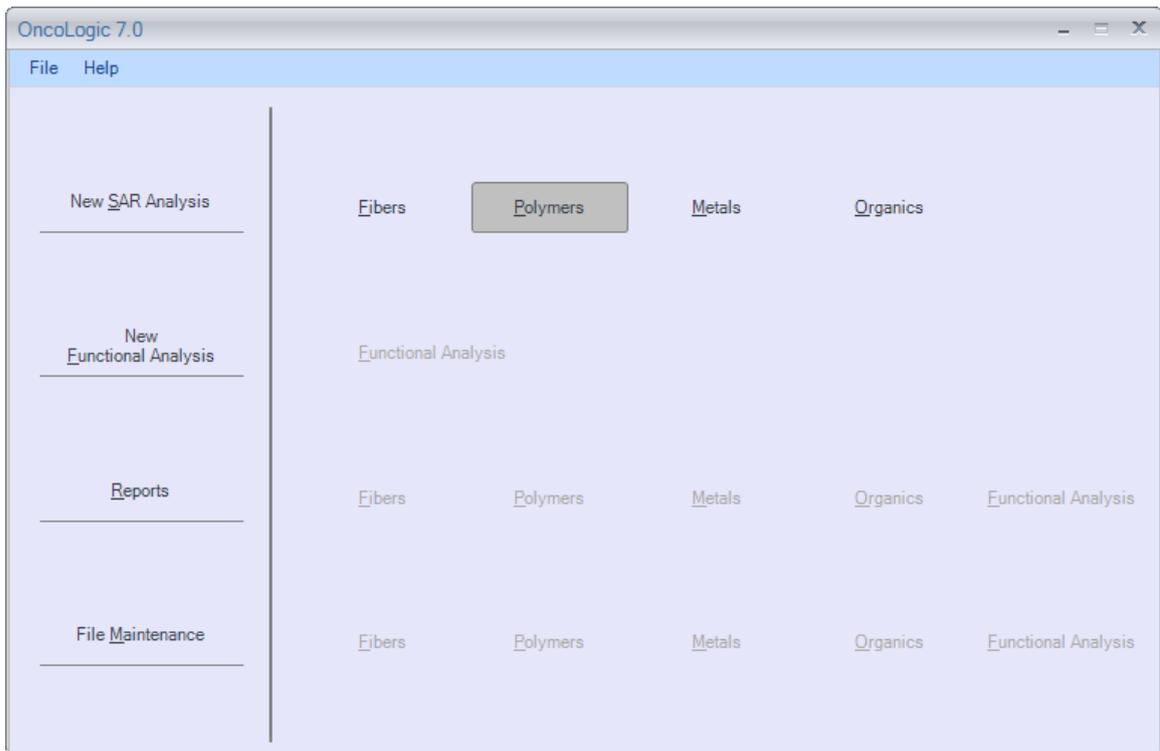
The final level of concern for the carcinogenic potential of this fiber is MODERATE.

<ESC> = Exit

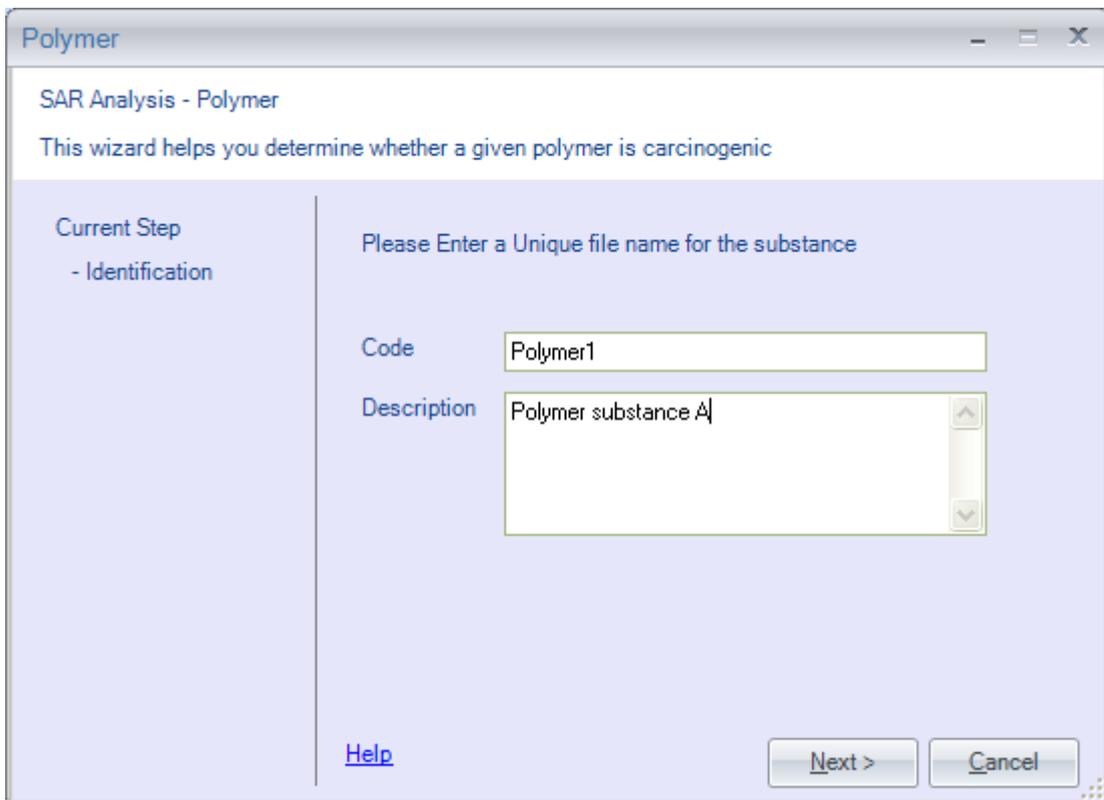
Press <Close> to return to main menu.

3.2. Running Polymer Module

- Polymer must consist of covalently linked repeating units and have a number average molecular weight >1000
- Questions may request information on
 - Percentage of polymer with MW <500 and <1000
 - Percent of residual monomer
 - Identification of reactive functional groups (RFGs)
 - Solubility
 - Special features (e.g., poly-function, water-solubility)
 - Exposure routes
 - Breakdown products (e.g., hydrolysis)



Select Polymers.



Enter the filename: Polymer1.

If a filename was used before, you will be asked to enter a different filename.

Enter: Polymer substance A

Press: <Next> when you are ready to continue.

You may enter any type of character for the substance identification. There is a limit of 240 letters, numbers, etc. that may be entered. Any more than 240 characters will not be accepted.

The screenshot shows a window titled "Polymer" with a subtitle "SAR Analysis - Polymer". Below the subtitle, it says "This wizard helps you determine whether a given polymer is carcinogenic". The window is divided into two main sections. On the left, under "Current Step", it says "- Number screen". On the right, the instruction reads "Please enter the number average molecular weight." Below this instruction is a text input field containing the number "1000". At the bottom of the window, there are three buttons: "< Back", "Next >" (which is highlighted in a darker shade), and "Cancel". A blue "Help" link is also visible near the bottom left of the main content area.

Enter the molecular weight: 1100.

Press: <Next>.

Polymer

SAR Analysis - Polymer

This wizard helps you determine whether a given polymer is carcinogenic

Current Step
- Covalently link

Does the substance consist of covalently linked repeating subunits?

Yes
 No

[Help](#)

< Back Next > Cancel

Select: Yes, and press “Next”.

Polymer

SAR Analysis - Polymer

This wizard helps you determine whether a given polymer is carcinogenic

Current Step
- Two percent

Does the polymer contain residual monomers exceeding 2 percent?

Yes
 No
 Unknown

[Help](#)

< Back Next > Cancel

Select: No, and press “Next”

Polymer

SAR Analysis - Polymer

This wizard helps you determine whether a given polymer is carcinogenic

Current Step
- Weight less than 500

Do more than 2 percent of the polymer molecules have a molecular weight less than 500?

Yes
 No
 Unknown

[Help](#)

< Back Next > Cancel

Select: Yes, and press "Next"

Polymer

SAR Analysis - Polymer

This wizard helps you determine whether a given polymer is carcinogenic

Current Step
- RFG Species

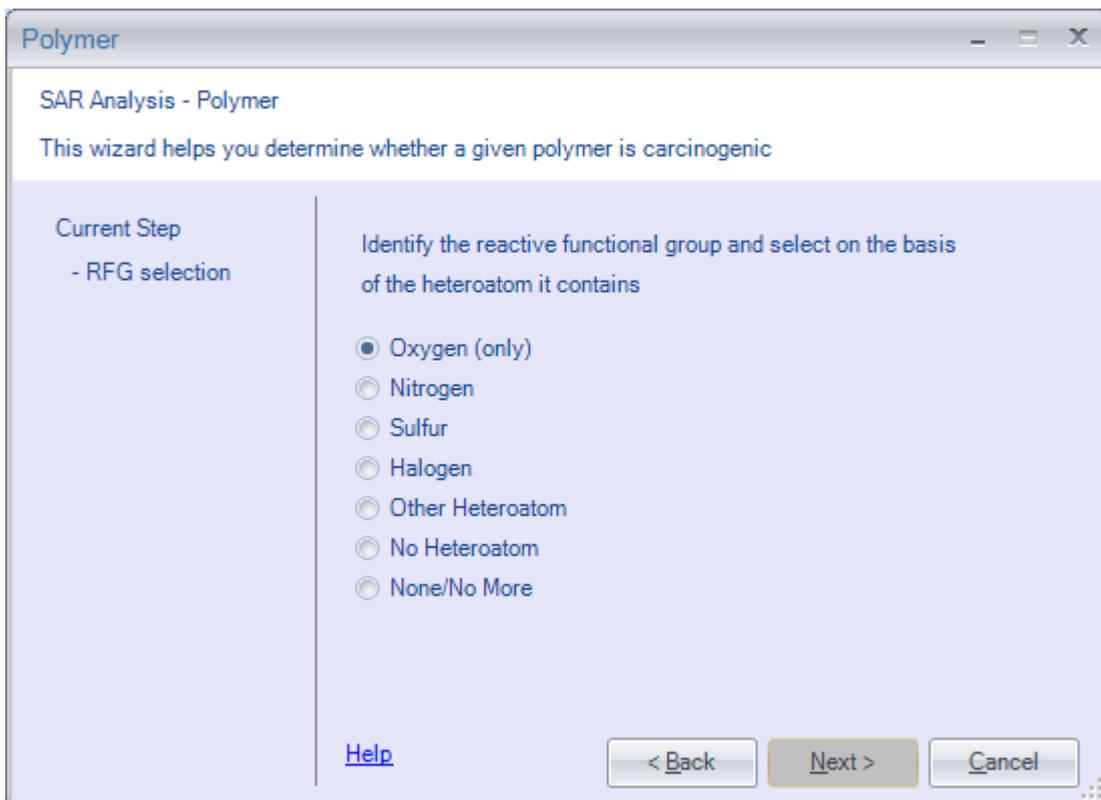
Does the low molecular weight species contain any reactive functional groups ?

Yes
 No
 Unknown

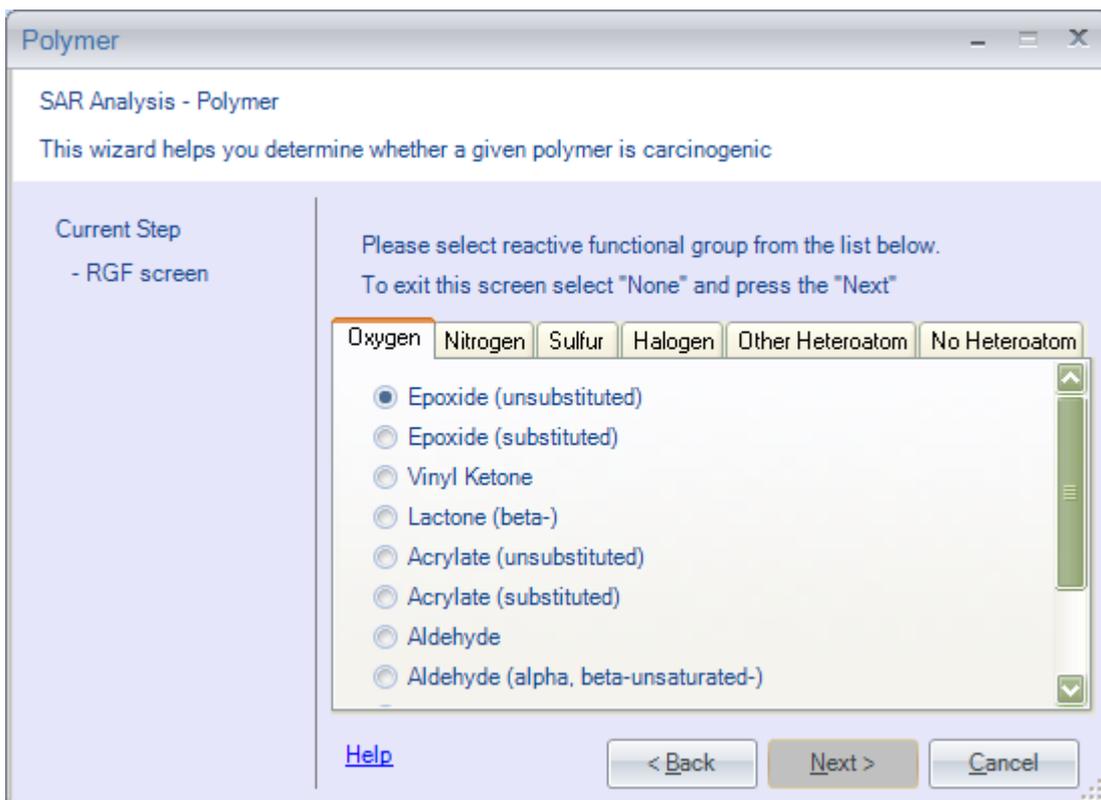
[Help](#)

< Back Next > Cancel

Select Yes, and press "Next"

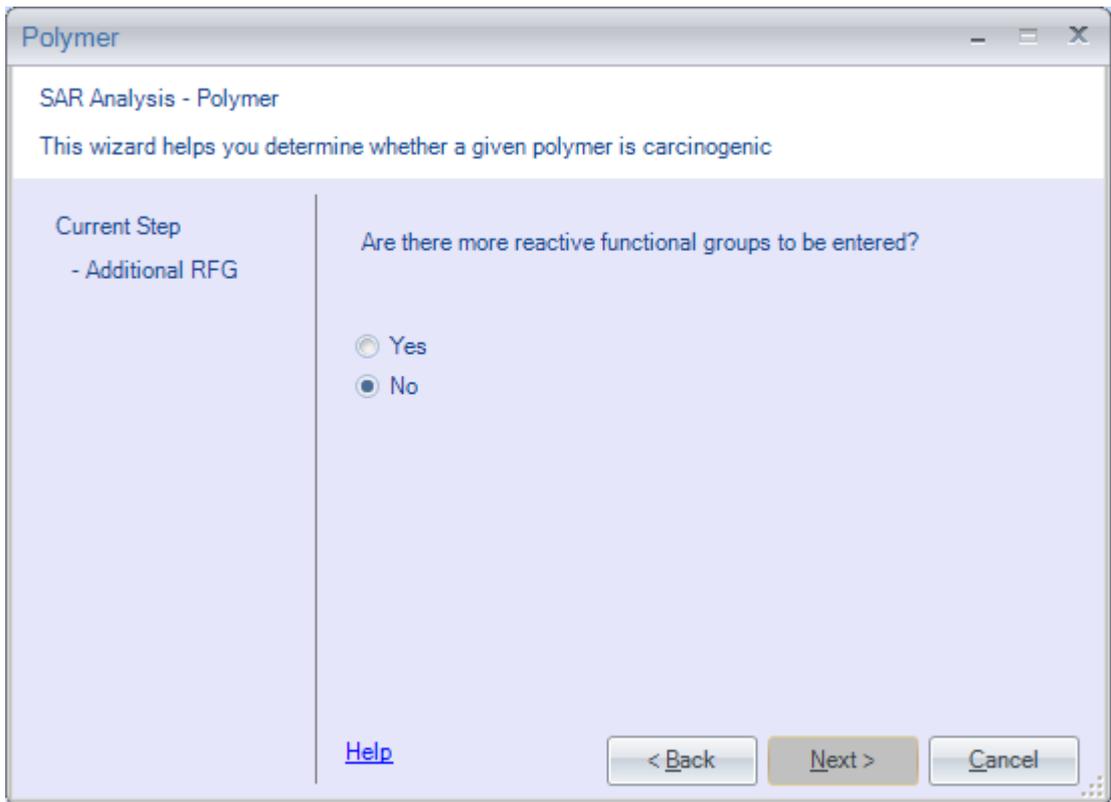


Select: Oxygen, and press Next

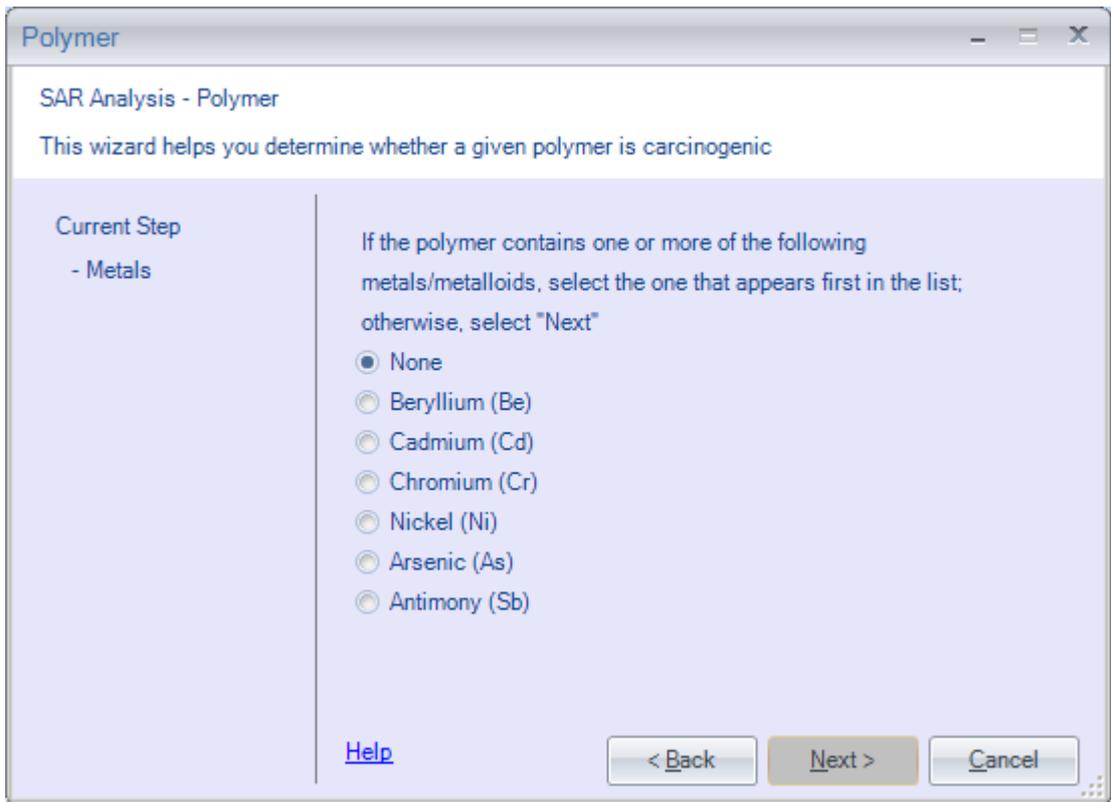


Select: Epoxide, and press "Next"

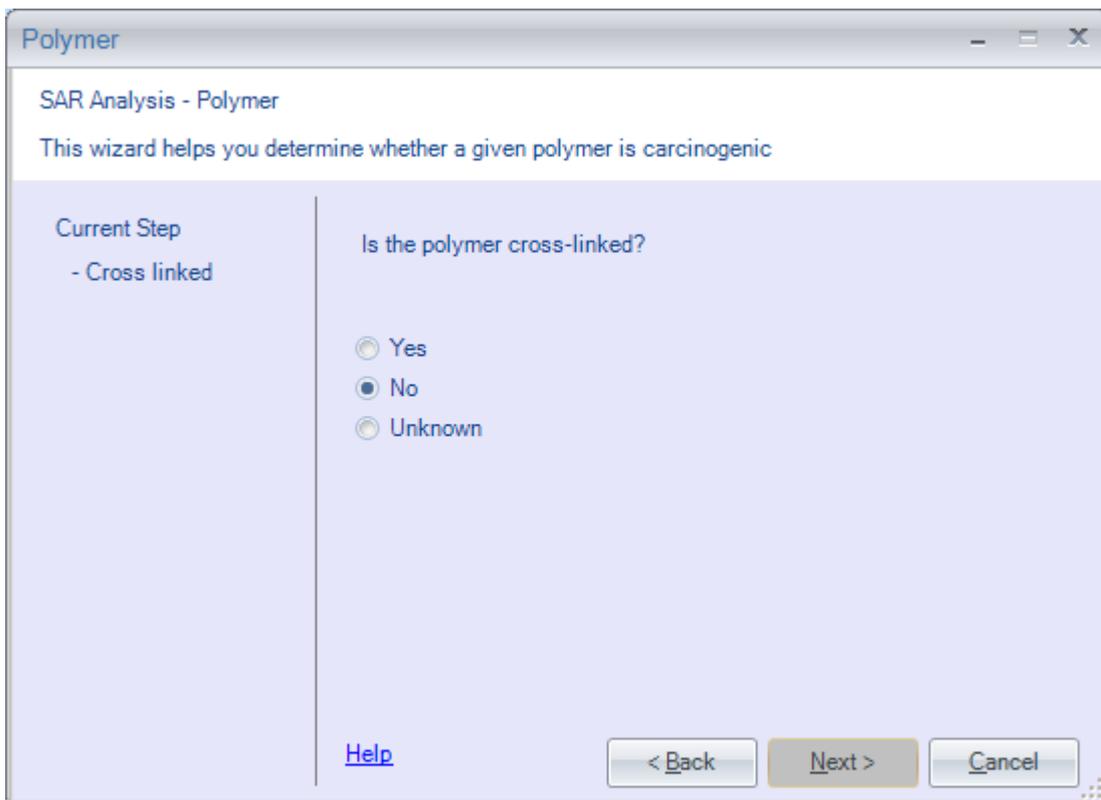
Note: On some of the RFG menus, it may be necessary to press the <Page Down> key in order to view all of the options.



Select: No, and press “Next”

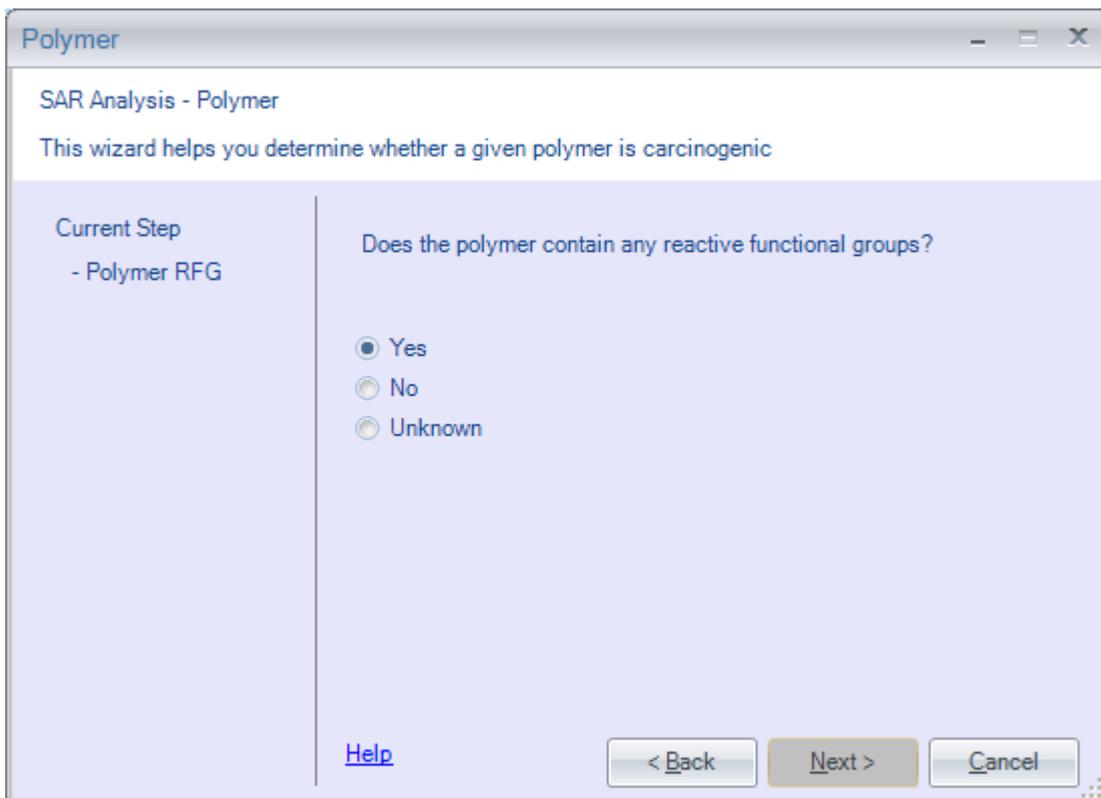


Select: None, and press “Next”

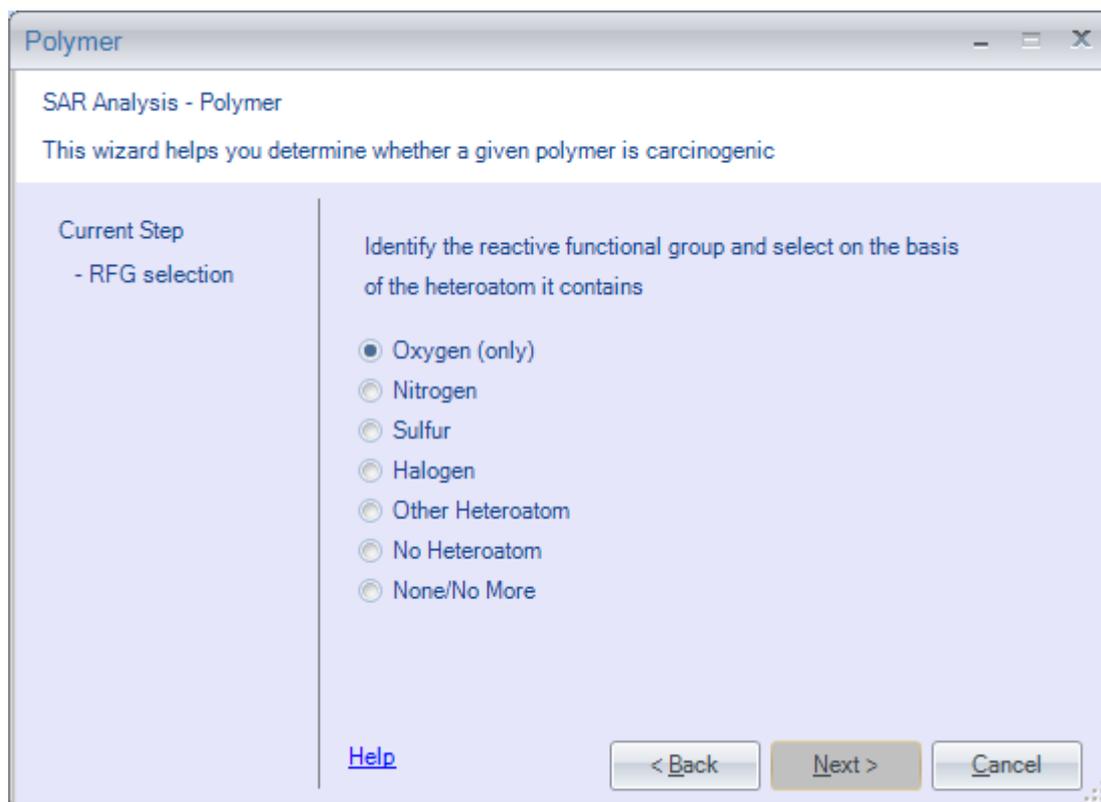


Select: No, and press "Next"

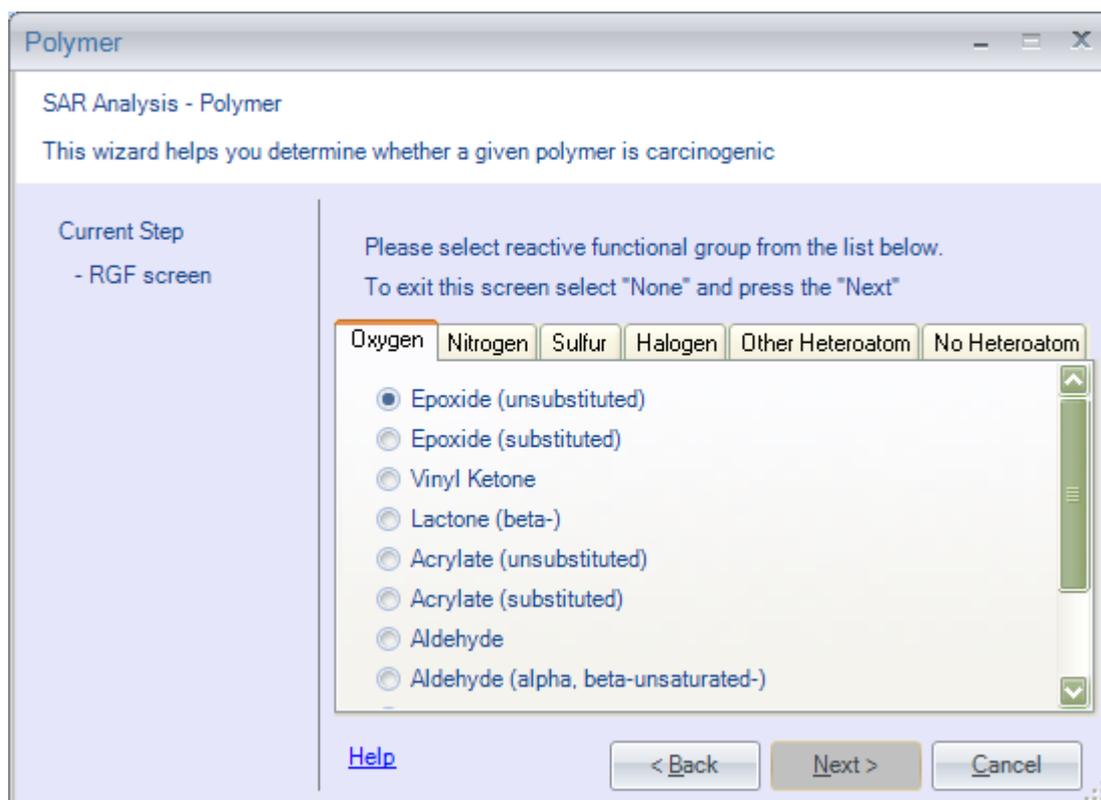
Note: Usually crosslinking can be determined by examining the structure of the polymer.



Select: Yes, and press "Next"



Select: Oxygen, and press "Next"



Select: Epoxide, and press "Next"

Polymer

SAR Analysis - Polymer

This wizard helps you determine whether a given polymer is carcinogenic

Current Step
- Additional RFG

Are there more reactive functional groups to be entered?

Yes
 No

[Help](#)

< Back Next > Cancel

Select: No, and press “Next”

Polymer

SAR Analysis - Polymer

This wizard helps you determine whether a given polymer is carcinogenic

Current Step
- Water solubility

Enter the water solubility of the polymer as weight percent. If water solubility is given in ppm, convert to percent by dividing the number by 10,000. If the weight percent is unknown, enter 0.

0.2

[Help](#)

< Back Next > Cancel

Enter: 0.2

Press: <Next>

Polymer

SAR Analysis - Polymer

This wizard helps you determine whether a given polymer is carcinogenic

Current Step
- Functional

Is the polymer polyfunctional?

Yes
 No

[Help](#)

< Back Next > Cancel

Select: Yes, and press “Next”

Note: Refer to the structure to determine if the reactive functional group occurs more than once in the polymer.

Polymer

SAR Analysis - Polymer

This wizard helps you determine whether a given polymer is carcinogenic

Current Step
- RFG Equivalent Weight

Considering the reactive functional group
Epoxide (unsubstituted)
enter the functional group equivalent weight.

550

[Help](#)

< Back Next > Cancel

Enter: 550

Press: <Next>

Polymer

SAR Analysis - Polymer

This wizard helps you determine whether a given polymer is carcinogenic

Current Step
- Interjunction Distance

Are the points of linkage of the Epoxide (unsubstituted) reactive functional groups to the polymer backbone separated by a distance of less than 10 atoms? Treat aromatic rings as 2.5 atoms and aliphatic rings as the number of atoms in the ring.

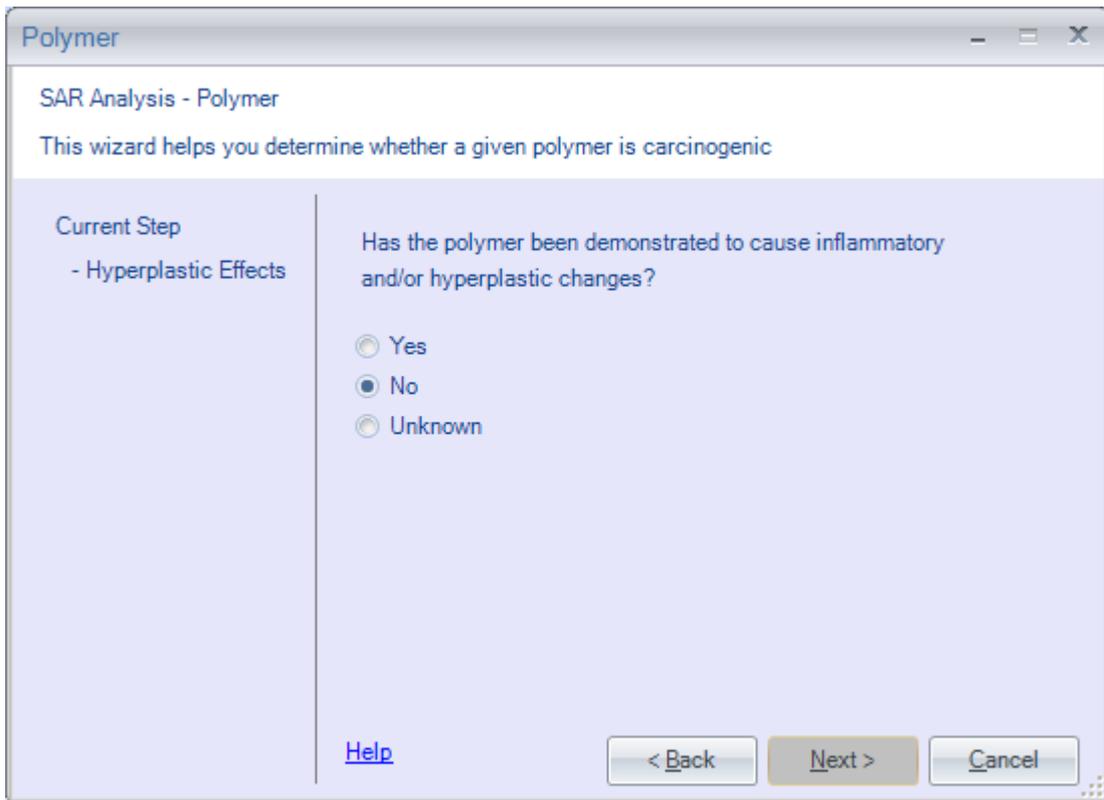
Yes
 No
 Unknown

[Help](#)

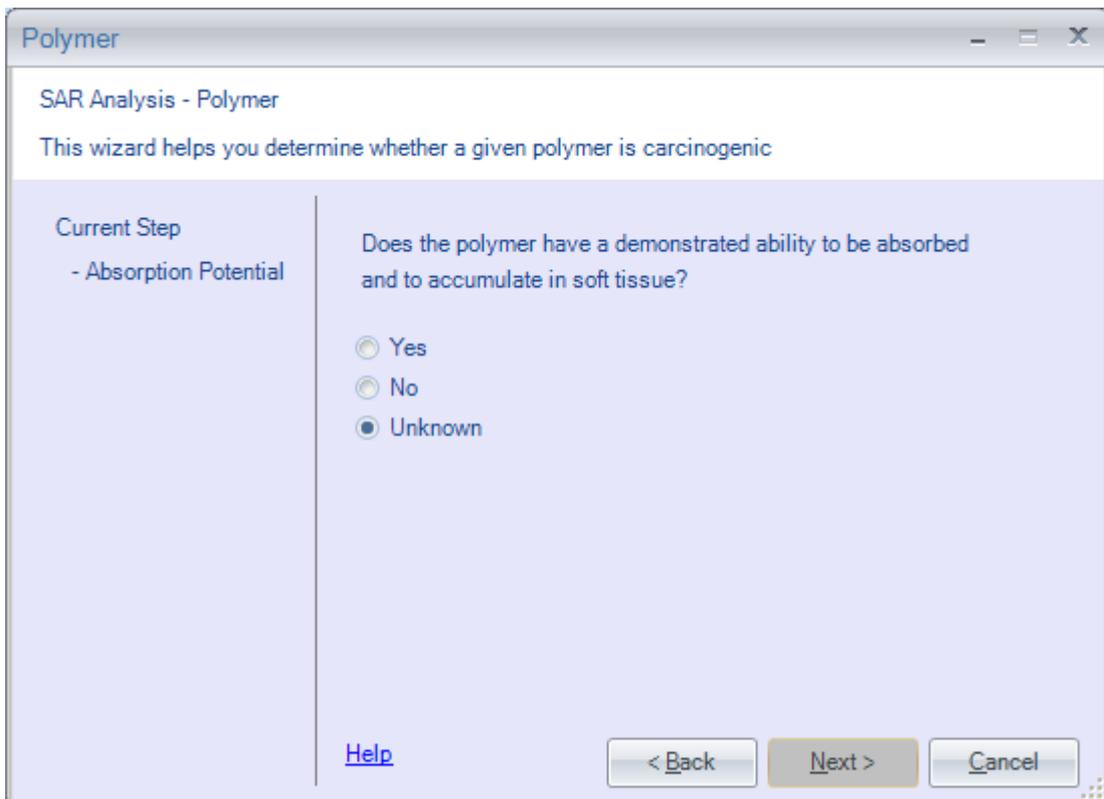
< Back Next > Cancel

Because the size of the polymer backbone is given as a range, we will use the average distance between the reactive functional groups. So, for $n = 2$, we get 7 atoms, and when for $n = 3$, we get 10 atoms. Averaging, we have 8.5 atoms. So, we will answer yes to the current question.

Select: Yes. , and press “Next”



Select: No, and press "Next"



Select: Unknown, and press "Next"

Polymer

SAR Analysis - Polymer

This wizard helps you determine whether a given polymer is carcinogenic

Current Step
- Ingestion

Is the polymer likely to be ingested?

Yes
 No

[Help](#)

< Back Next > Cancel

Select: Yes, and press “Next”

Polymer

SAR Analysis - Polymer

This wizard helps you determine whether a given polymer is carcinogenic

Current Step
- Internal Releasable
Subunits

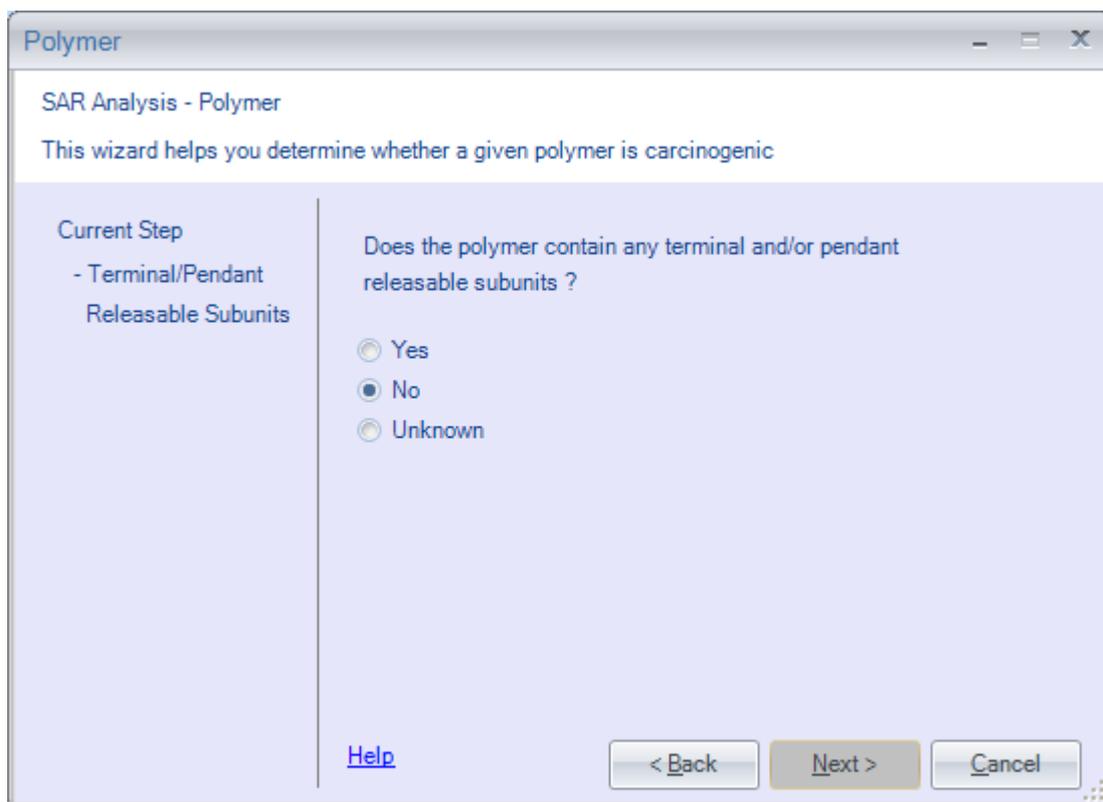
Does the polymer contain any internal releasable subunits?

Yes
 No
 Unknown

[Help](#)

< Back Next > Cancel

Select: No, and press “Next”



Select: No, and press “Next”

At this point, the evaluation will be complete, and the justification report displayed. Because the justification report is more than one page long, you will need to scroll down to read the entire report. This can be accomplished in two ways. You may press the <Page Down> key or you can use the mouse and move the pointer to the right hand side of the window and click on the arrows to scroll the text. The screens that follow will contain the justification report a page at a time as if someone was using the <Page Down> key to scroll.

Justification Report

OncoLogic Justification Report

SUMMARY :

Filename : Polymer1

Substance ID : Polymer substance A

The final level of carcinogenicity concern for this polymer is LOW-MODERATE.

Based on the reactive functional group Epoxide (unsubstituted), the level of concern for the low molecular weight species is LOW-MODERATE.

CAUTIONARY NOTES: 1. Plasticizers and other additives, if present, should be evaluated separately in the Organics Subsystem. 2. Counterions of polymers with ionic backbones should be evaluated separately.

JUSTIFICATION:

Because the substance consists of covalently linked repeating units and has a molecular weight greater than or equal to 1000, the substance is classified as a high molecular weight polymer.

Since the polymer contains less than 2% residual monomer(s), the carcinogenicity concern for any residual monomers is LOW.

The polymer contains low molecular weight species (>2% below 500), with a reactive-functional-group-bearing sidechain. The level of carcinogenicity concern for the low molecular weight species is based on the reactive functional group: Epoxide (unsubstituted). The level of carcinogenicity concern for the low molecular weight species is LOW-MODERATE.

The polymer is not cross-linked.

Justification Report

Since the percent water solubility is greater than or equal to 0.1%, the polymer is considered to be soluble in water.

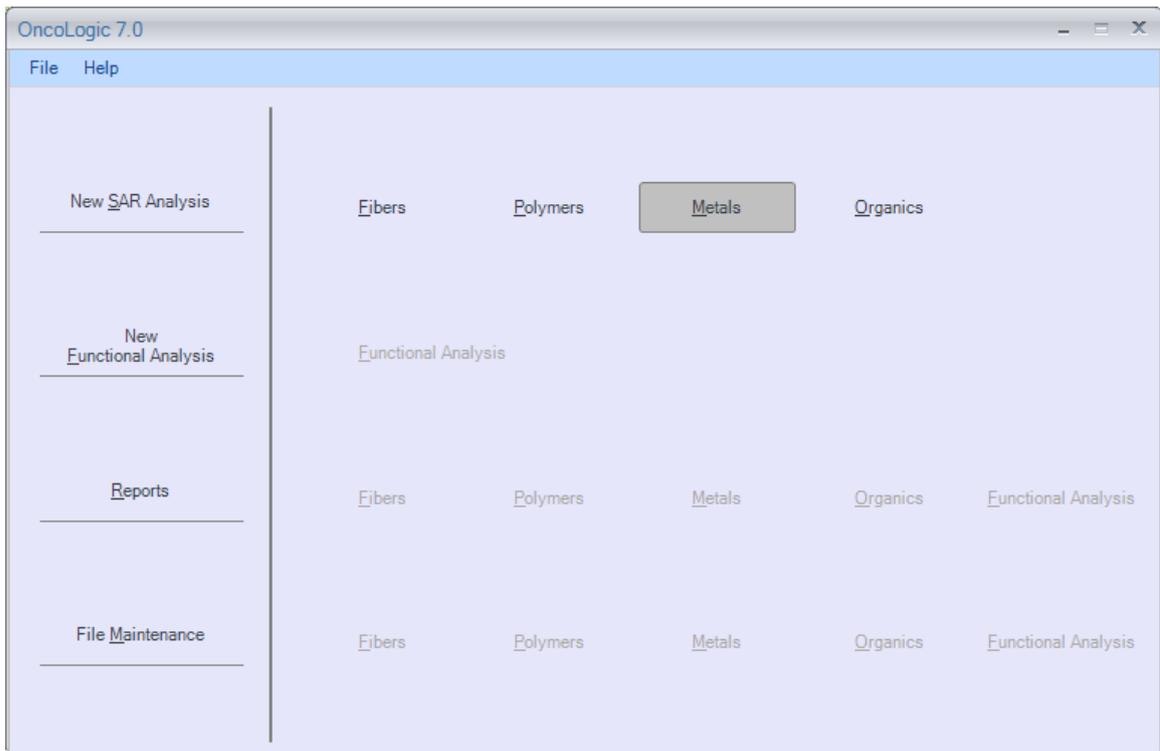
The reactive functional group (RFG) which was used during the evaluation of the polymer is: Epoxide (unsubstituted).

This water soluble polymer is polyfunctional. Based on the expert-assigned inherent carcinogenic potential of the RFG(s) that you have entered and the entered information on the functional group equivalent weight of 550 daltons, which is low enough to cause concern, and the interjunction distance of less than ten atoms, which is within the favorable distance for potential cross-linking, the RFG which is retained for the evaluation of the polymer is: Epoxide (unsubstituted). Since the polymer has been demonstrated not to cause (or is not known to have caused) inflammatory and/or hyperplastic changes, carcinogenicity concerns arising from these pathophysiological changes can be eliminated. The RFG which is contained in this polymer is known to be stable in solution or as an emulsion in water. The current level of carcinogenicity concern based on the RFG is retained.

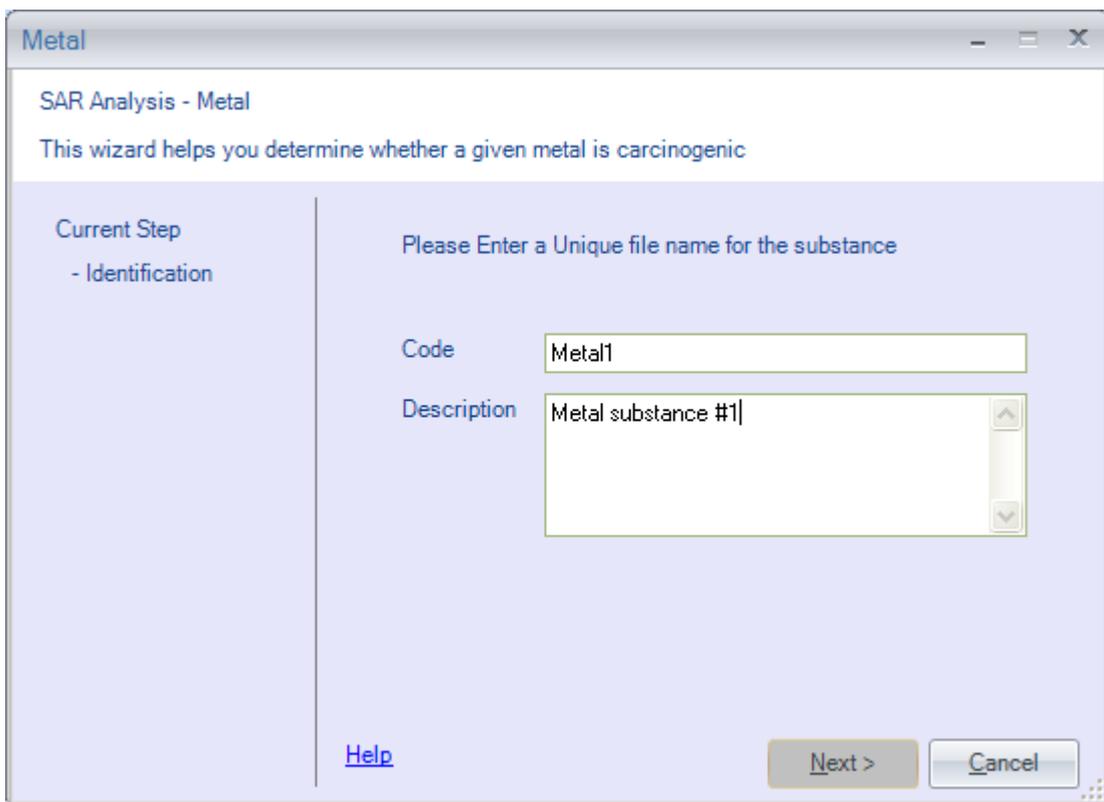
The water soluble polymer has a molecular weight less than or equal to 2500. The polymer contains reactive-functional-group-bearing sidechains but has not (or is not known to have) demonstrated an ability to be absorbed and to accumulate in soft tissue. Therefore, the level of carcinogenicity concern for this polymer is LOW-MODERATE.
The final concern for this polymer is LOW-MODERATE.

Press: <Close>. This will return you to the main menu.

3.3. Running Metals Module



Select: Metals



Enter the filename: Metal1.

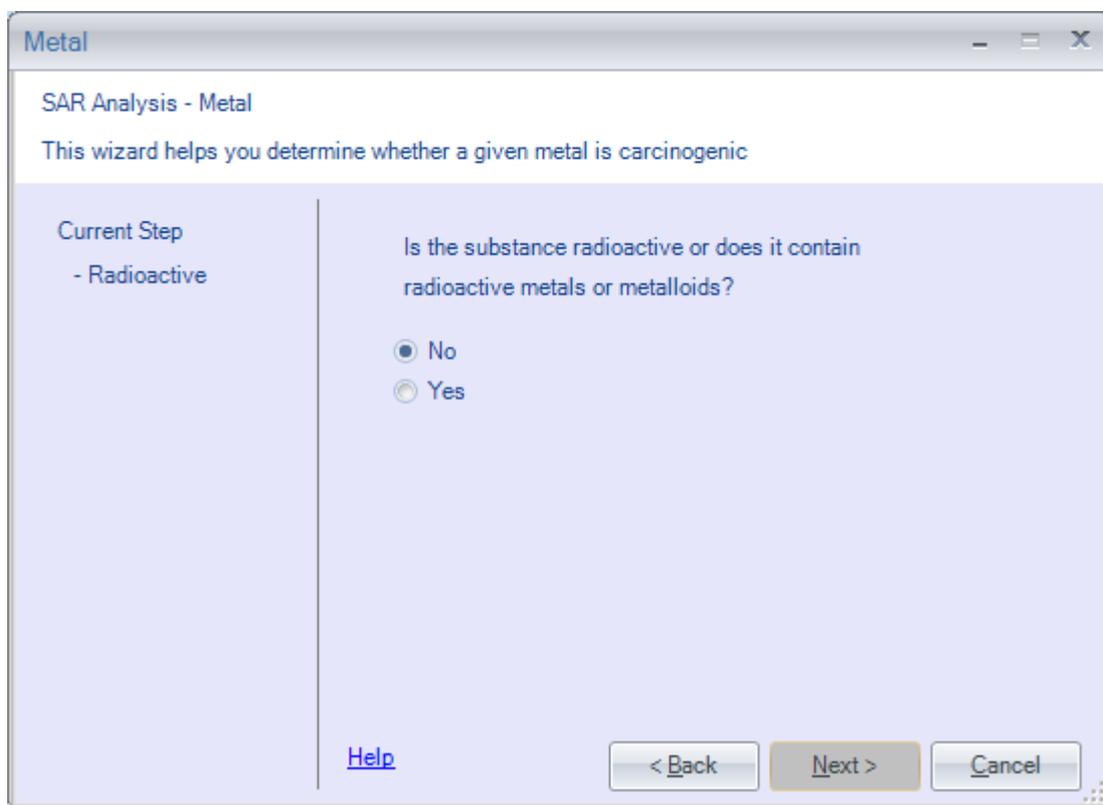
If a filename was used before, you will be asked to enter a different filename.

Enter: Metal substance #1

You may change what you have typed by using the <Backspace> key.

Press: <Next> when you are ready to continue.

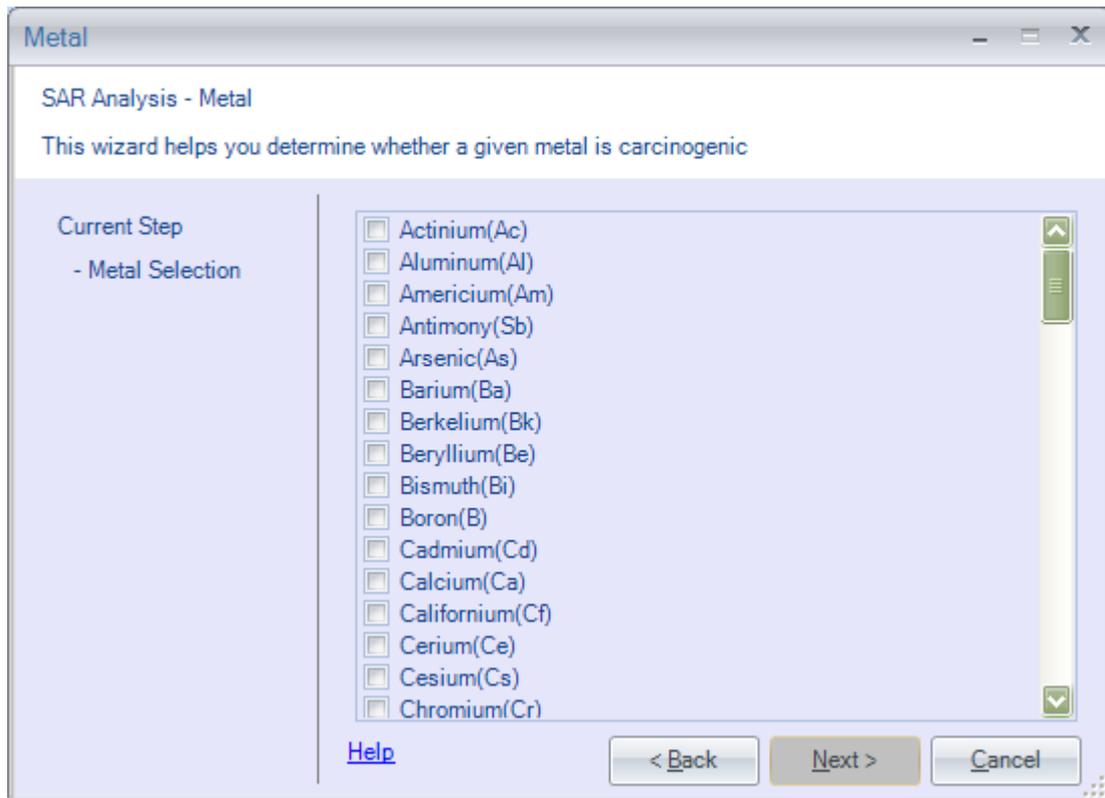
You may enter any type of character for the substance identification. There is a limit of 240 letters, numbers, etc. that may be entered. Any more than 240 characters will not be accepted.



The screenshot shows a software window titled "Metal" with a subtitle "SAR Analysis - Metal". The main text reads: "This wizard helps you determine whether a given metal is carcinogenic". On the left side, under "Current Step", it says "- Radioactive". The main area contains the question: "Is the substance radioactive or does it contain radioactive metals or metalloids?". There are two radio button options: "No" (which is selected) and "Yes". At the bottom, there is a "Help" link, and three buttons: "< Back", "Next >" (highlighted in yellow), and "Cancel".

Select: No.

If you had answered Yes, the evaluation would have end. The metals subsystem is not designed to evaluate radioactive substances.



Select Chromium and Zirconium and press “Next”

Metals which do not appear in the initial window screen can be viewed by scrolling down. To scroll down either press the <Page Down> key or use the mouse to click the arrows on the right hand side of the screen. Another way to quickly move near a desired metal is to press the first letter of the metal name. The highlighted box will then move to the first metal containing the pressed letter. Continuing to press the first letter will cause the highlight bar to advance through the metals beginning with that letter.

Metal

SAR Analysis - Metal

This wizard helps you determine whether a given metal is carcinogenic

Current Step
- Metallized dye

Is the substance in the form of a metallized dye or pigment?

Yes
 No

[Help](#)

< Back Next > Cancel

Select: No

Metal

SAR Analysis - Metal

This wizard helps you determine whether a given metal is carcinogenic

Current Step
- Metal substance
classification

Classify the type of metal-containing substance.

Metal dust
 Carbonyl-type compound
 Complex or Coordination compound
 Inorganic or Other Organic compound

[Help](#)

< Back Next > Cancel

Select: Inorganic or Other compound.

Since the compound being evaluated does not fall into the first three categories, the fourth category, Inorganic/Other, is selected.

Metal

SAR Analysis - Metal

This wizard helps you determine whether a given metal is carcinogenic

Current Step
- Chromium oxidation state

Select the oxidation state of the Chromium.

Divalent
 Trivalent
 Hexavalent

[Help](#)

Select: Hexavalent.

Metal

SAR Analysis - Metal

This wizard helps you determine whether a given metal is carcinogenic

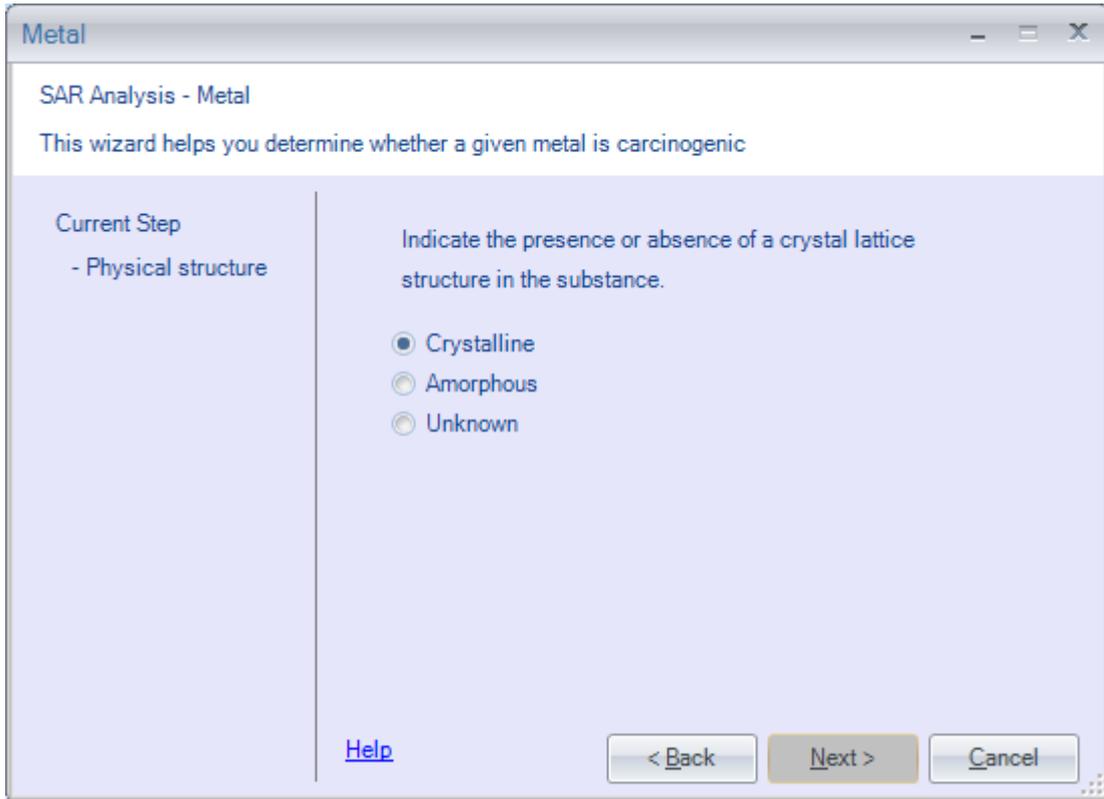
Current Step
- Water solubility

Select the water solubility of the substance.

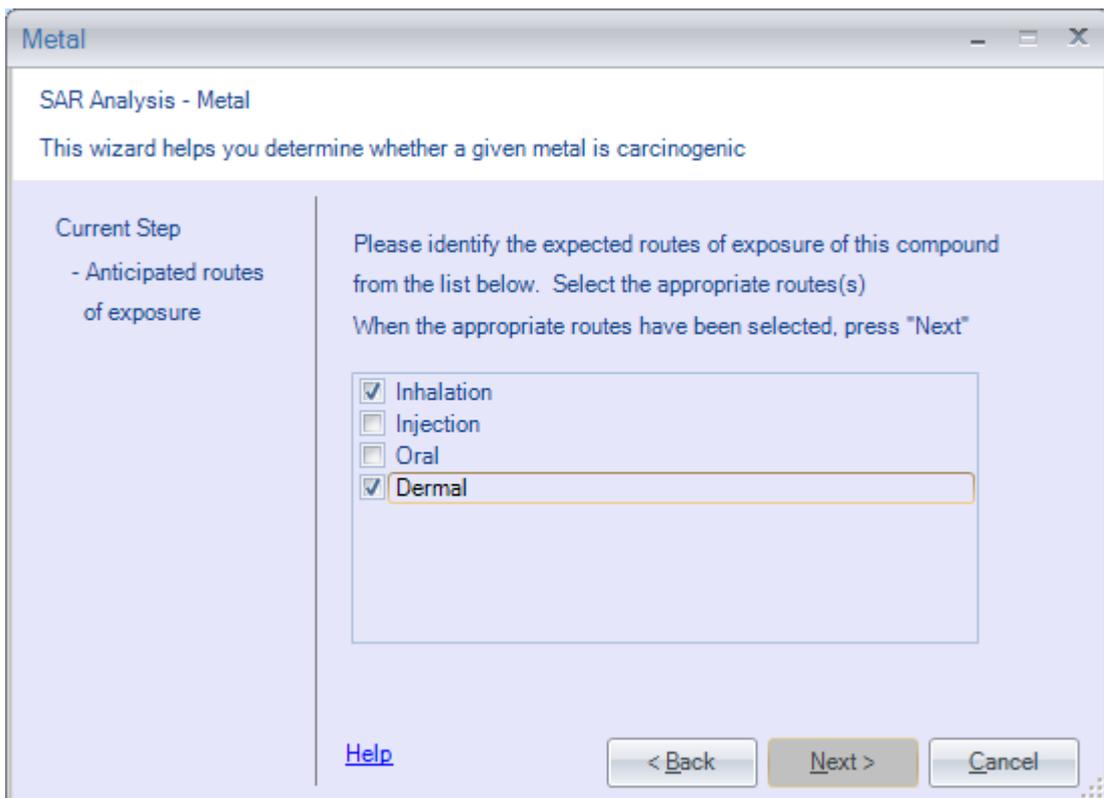
Soluble
 Sparingly Soluble
 Insoluble
 Unknown

[Help](#)

Select: Sparingly.



Select: Crystalline.



Select Inhalation and Dermal
Press <Next>.

Metal

SAR Analysis - Metal

This wizard helps you determine whether a given metal is carcinogenic

Current Step
- Organic moiety

Is the substance expected to release an organic moiety under physiological conditions, including the acidic condition of the stomach?

Yes
 No
 Unknown

[Help](#)

Select: No.

At this point, the evaluation will be complete, and the justification report displayed. Because the justification report is more than one page long, you will need to scroll down to read the entire report. This can be accomplished in two ways. You may press the <Page Down> key or you can use the mouse and move the pointer to the right hand side of the window and click on the arrows to scroll the text. The screens that follow will contain the justification report a page at a time as if someone was using the <Page Down> key to scroll.

Justification Report

OncoLogic Justification Report

SUMMARY :
Filename : Metall
Substance ID : Metal substance #1
The final level of concern for this Cr-containing inorganic or organic compound , when the anticipated exposure is via the inhalation route , is HIGH.

JUSTIFICATION

Since this substance contains more than one metal, Cr, Zr, the system has considered all metals present. The level of concern and the line of reasoning are based on the metal which provides the highest level of carcinogenicity concern. When more than one metal gives the same highest level of concern, the line of reasoning is given for only one of the metals.

In general, virtually all Cr-containing compounds are of some carcinogenicity concern unless they can be clearly shown to be not bioavailable. Exposure to these compounds by inhalation or injection is of greater concern than exposure by the oral or dermal route.

The carcinogenic potential of inorganic chromium compounds is affected by their oxidation state, crystallinity, and solubility, which affect the extent of compound uptake by cells. Hexavalent compounds are more easily taken up by cells than trivalent; and crystalline compounds are more easily taken up than amorphous compounds. Sparingly soluble and insoluble compounds are more likely than soluble compounds to be retained at the site of exposure, and thus have more of an opportunity to be taken up by the cells. Organic chromium compounds containing a Cr-C covalent bond are treated as inorganic compounds because the Cr-C covalent bond is expected to be easily hydrolyzed in aqueous solution.

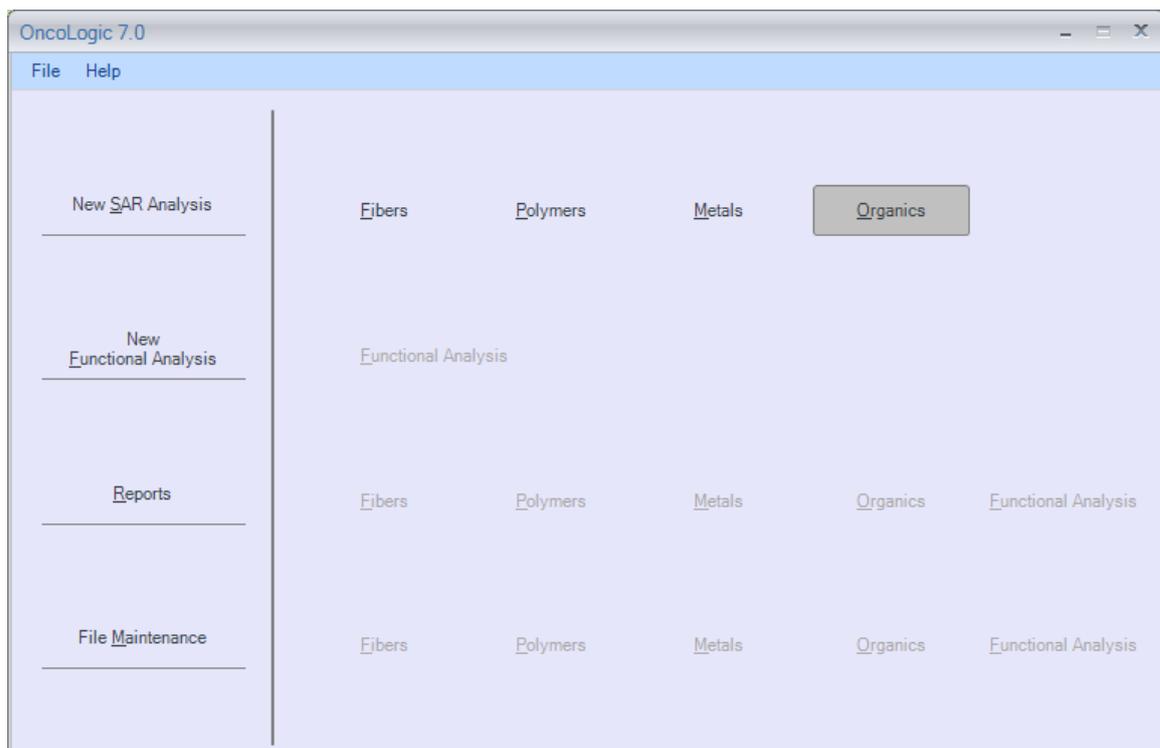
Justification Report

Since the substance is a(an) inorganic or organic compound, and the oxidation state of chromium is hexavalent, and exposure to this sparingly soluble, crystalline substance is expected to be by the inhalation route, the level of carcinogenicity concern is HIGH.

The final level of concern for this Cr-containing inorganic or organic compound , when the anticipated exposure is via the inhalation route , is HIGH.

Press: <Close> will return you to the main menu.

3.4. Running Organics Module



Select: Organics

Organics

SAR Analysis - Organics

This wizard helps you determine whether a given organics is carcinogenic

Current Step
- Basis of the Evaluation

Would you like to base the evaluation on a new compound or a compound that has been previously evaluated?

New Compound

Previously Evaluated Compound

[Help](#)

Next > Cancel

Select: New Compound

Organics

SAR Analysis - Organics

This wizard helps you determine whether a given organics is carcinogenic

Current Step
- Identification

Please Enter a Unique file name for the substance

Code: Amine1

Description: Aromatic amine #1

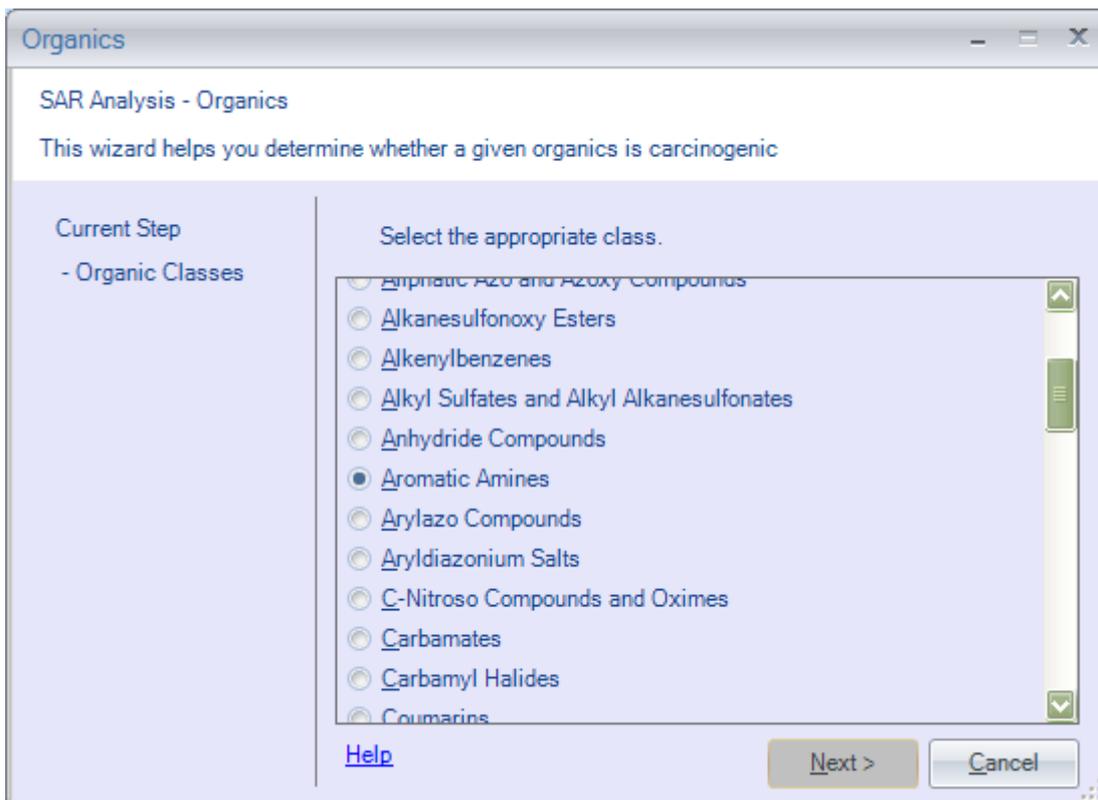
[Help](#)

Next > Cancel

Enter the filename: Amine1.

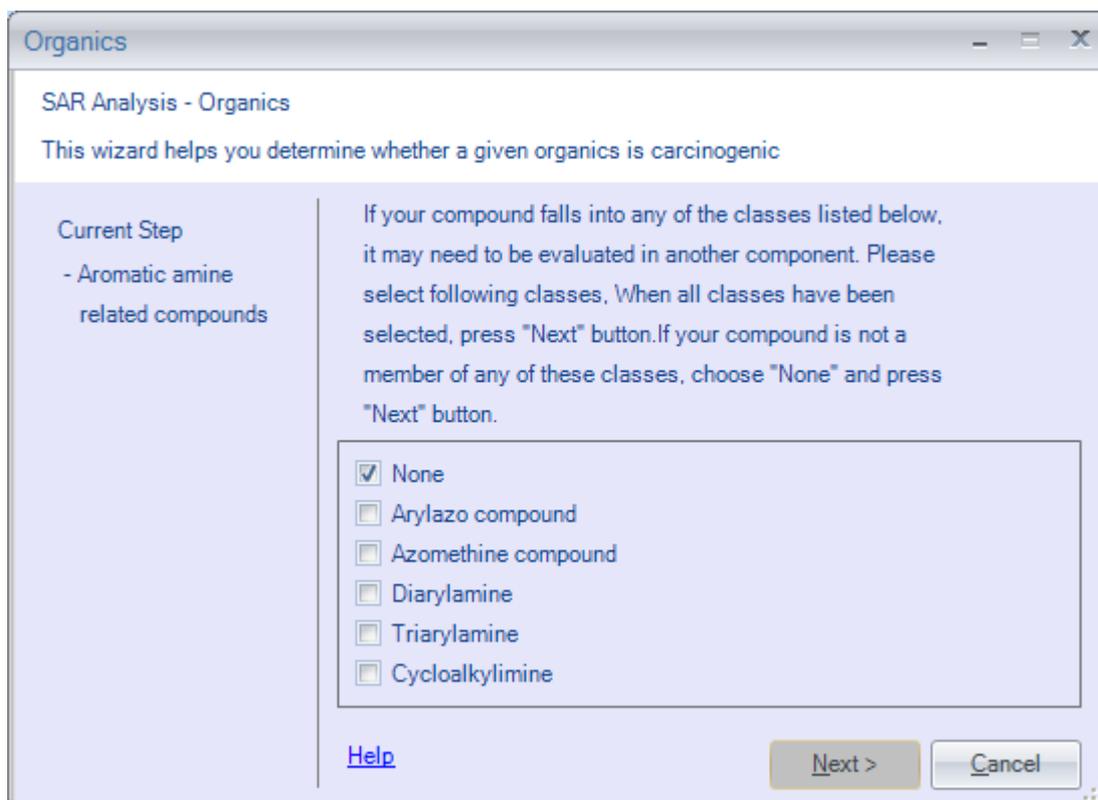
Press: <Next>

If a filename was used before, you will be asked to enter a different filename.

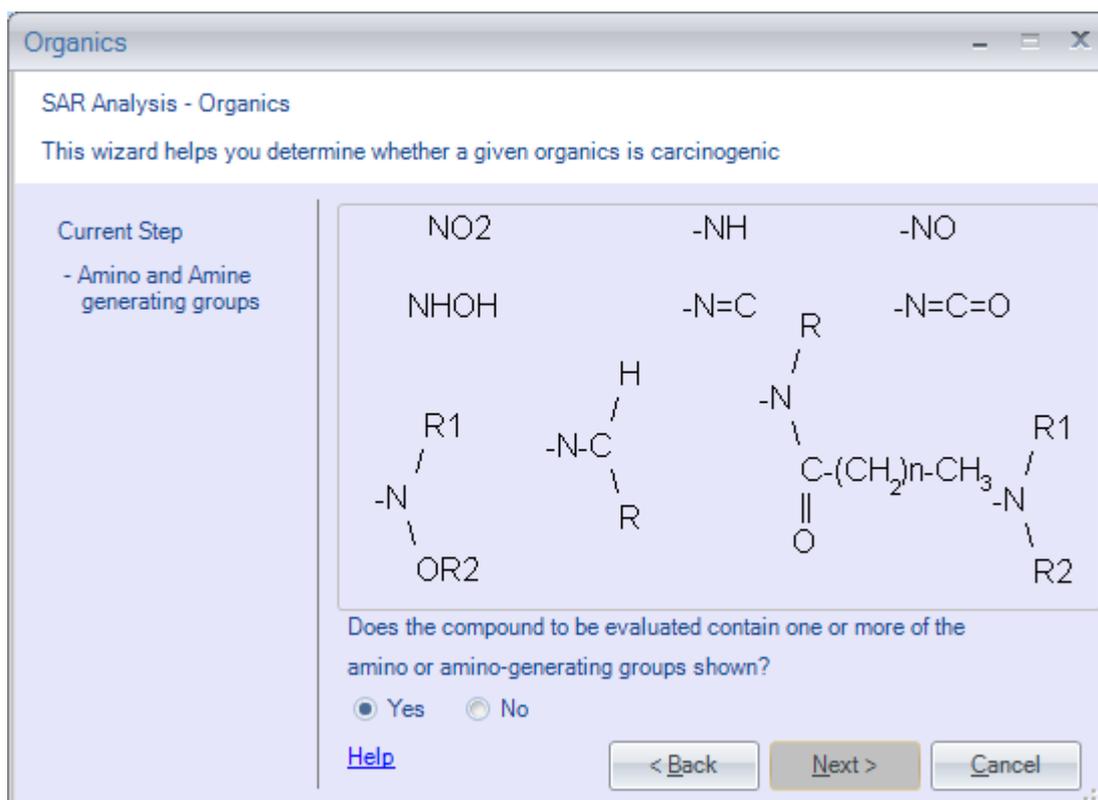


Select: Aromatic Amines.

Note: In order to see the other organic classes, you need to scroll down. This can be done by either pressing the <Page Down> key or using the mouse to click the arrows on the right hand side of the window. Also, by pressing the first letter of the organic class, the highlight bar will jump to the first class starting with that letter. By continually pressing that letter, the highlight bar will cycle through all of the organic classes beginning with that letter.

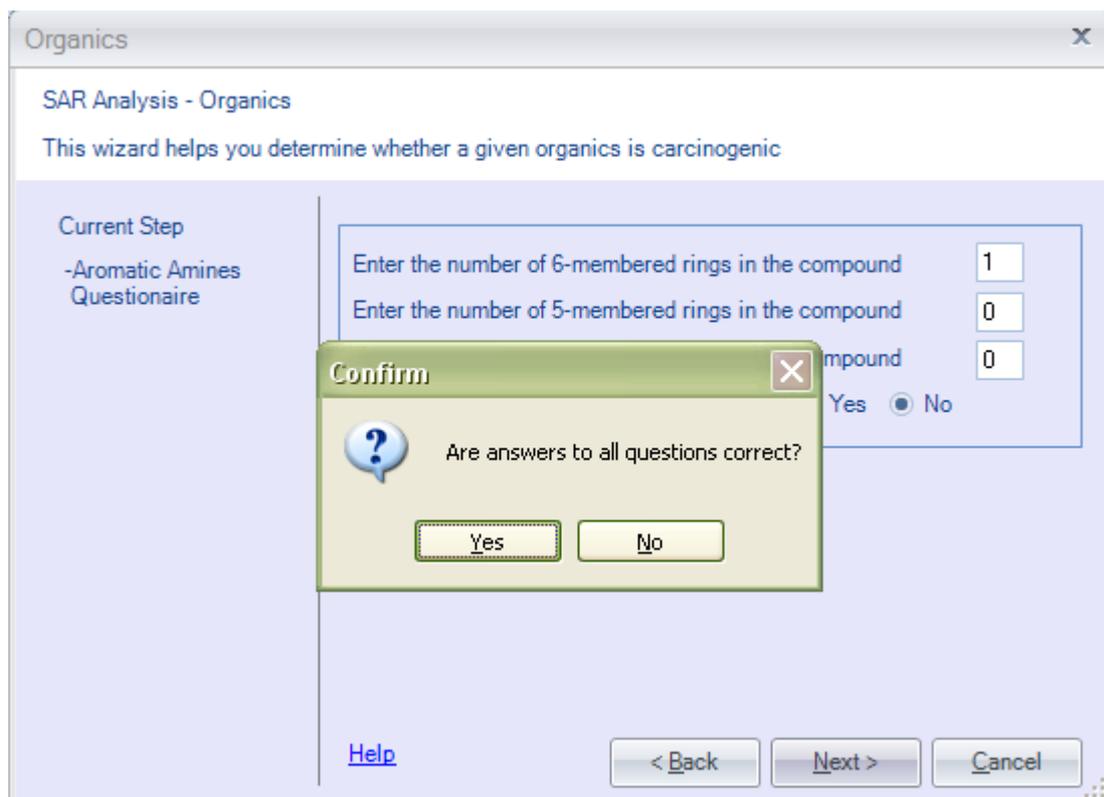


Select: NONE and **press** <Enter>.

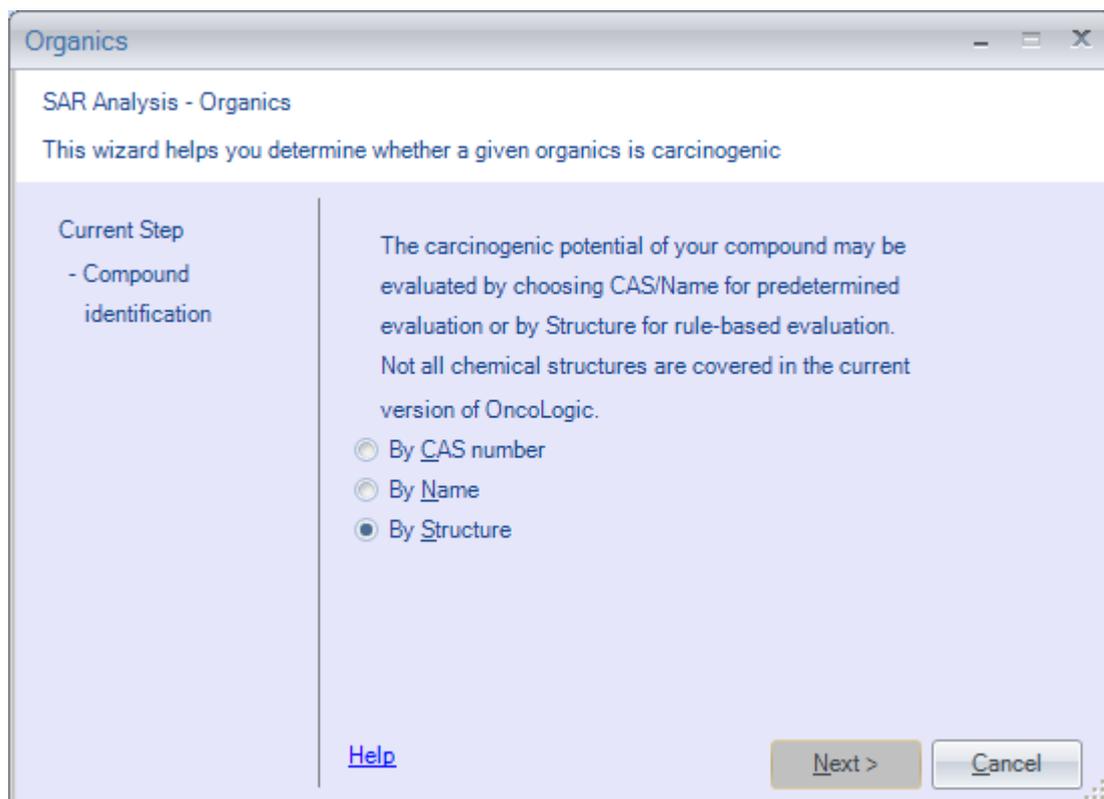


Select: Yes and **press** <Return>.

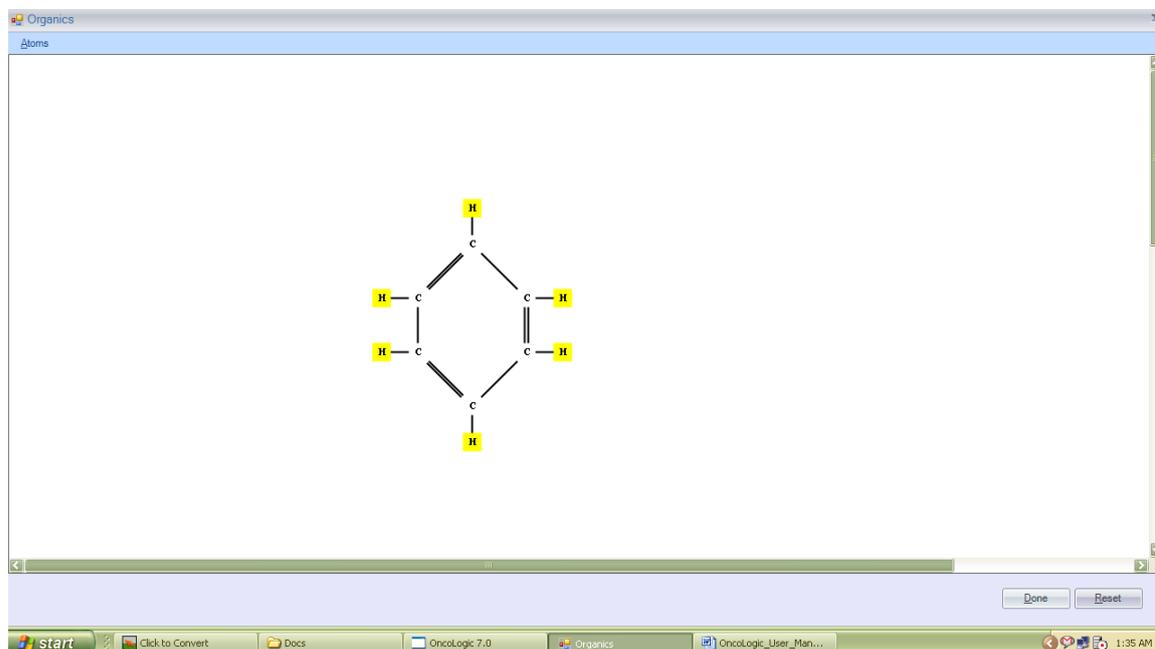
Highlight CONTINUE and **press** <Return> or **click** left mouse button.



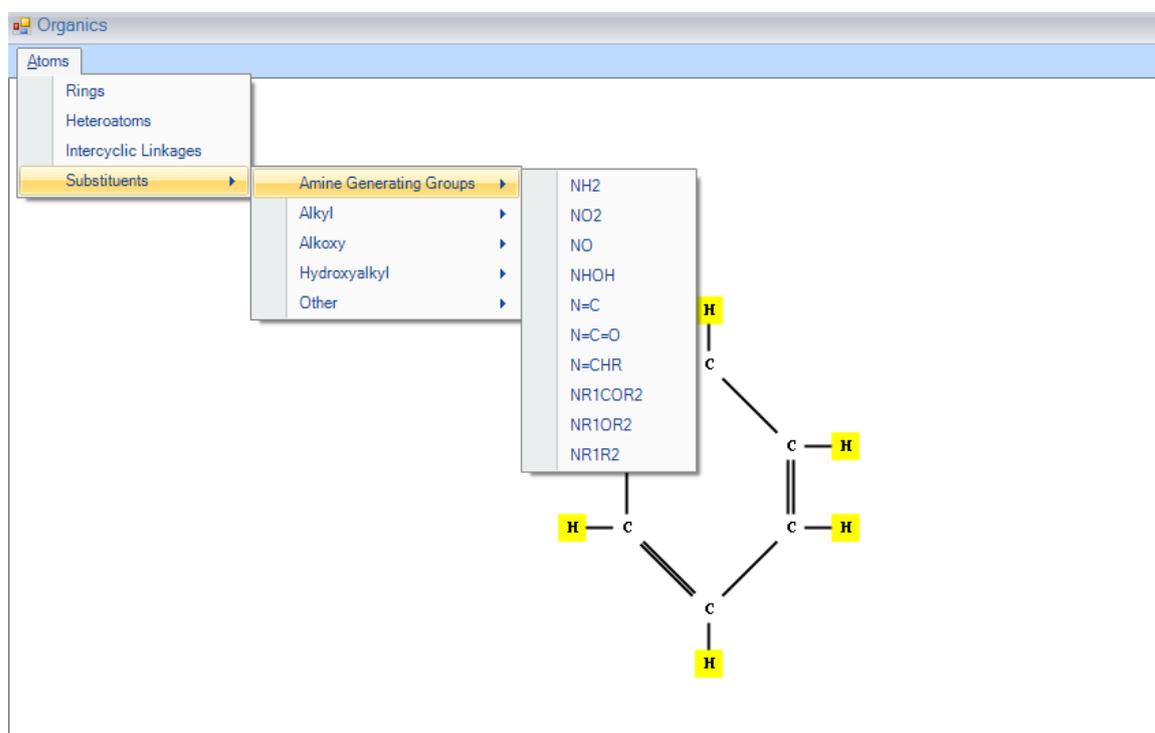
Fill the proper ring data and give answers to the Questionnaires.



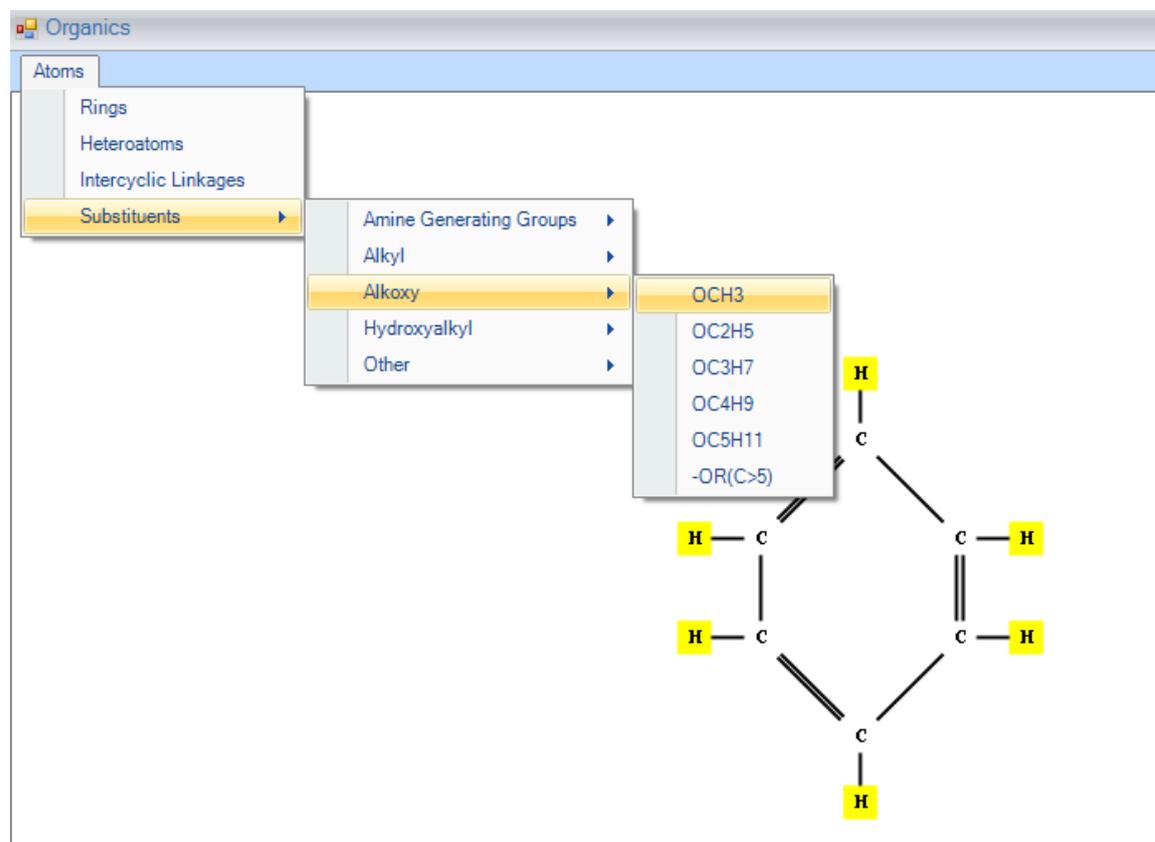
Because we do not have the name or CAS number for the compound, we will **select 'BY STRUCTURE'**. However, if the CAS number or name had been known, use of the database would have been the first course of action.



As before, the method using commands is accomplished through the use of pull down menus. For us to build the compound, we will begin by **selecting the 'Atoms' menu option and clicking** with the left mouse button.

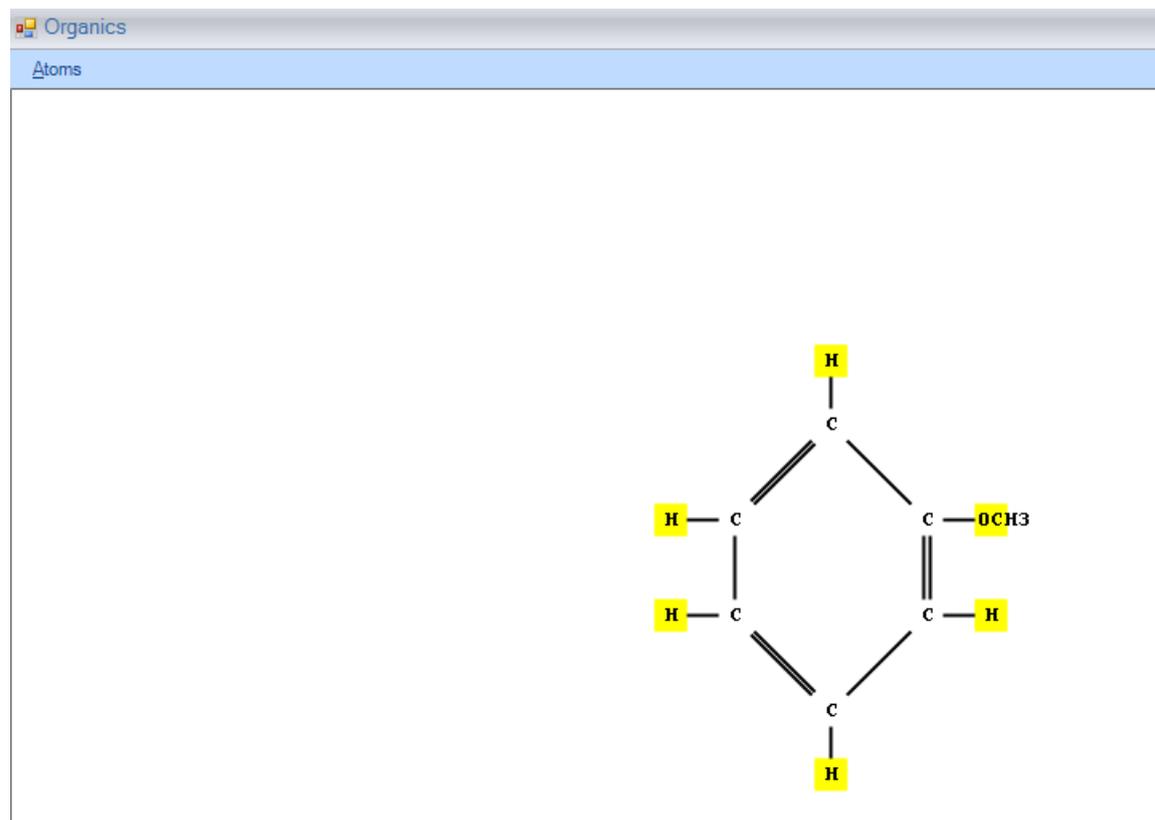


As you will see, there are now four more options which can be selected. We will **highlight Substituents** and **click** the mouse button.

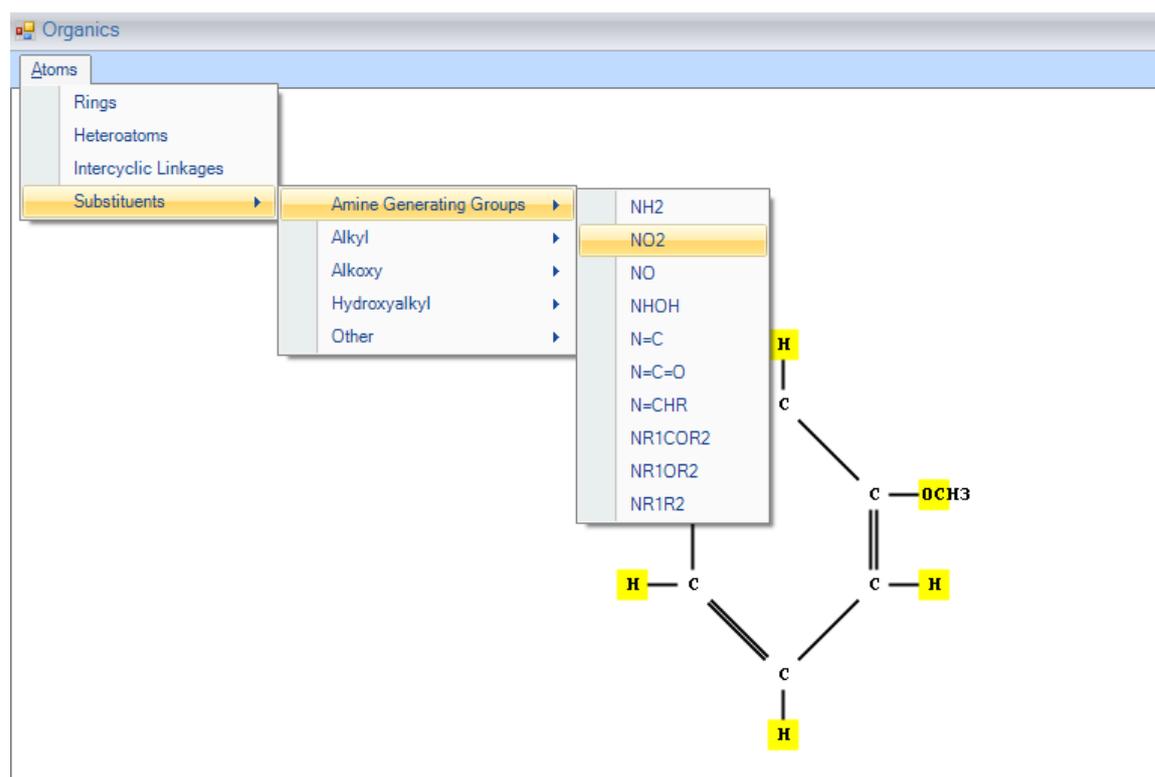


From here we will **highlight and select -OCH₃** by clicking the mouse button in order to add the substituent to the ring structure.

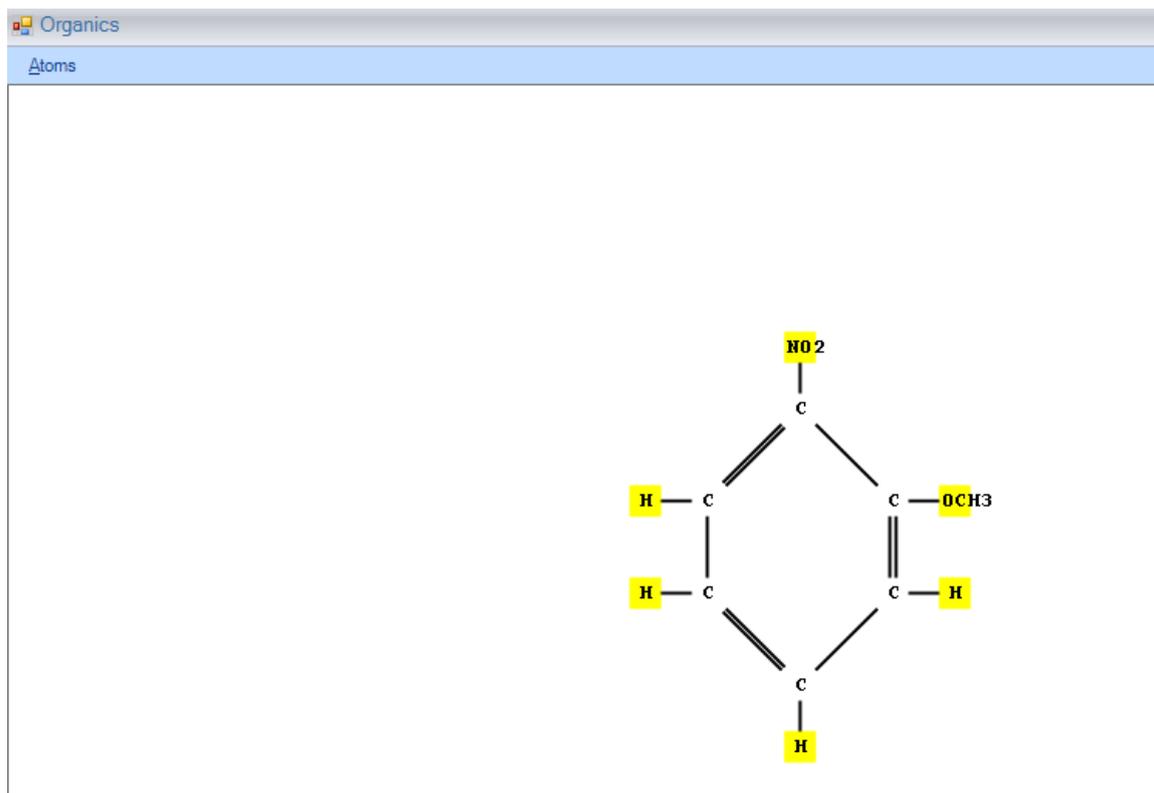
Once you have selected the substituent, you can then place it onto the skeleton using the mouse. First pick a location to add the substituent onto by **moving the mouse pointer over the appropriate atom, click** the left mouse button.



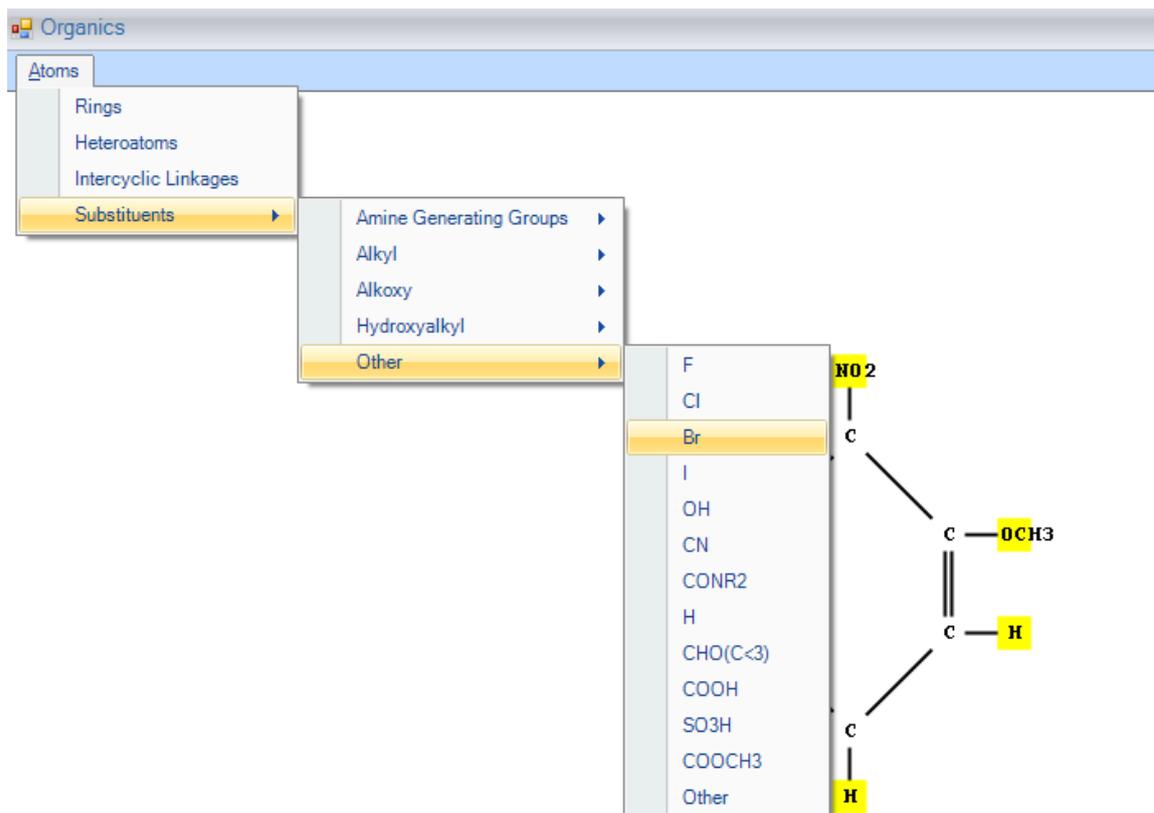
Since we have no other methoxy substituents to add to the compound. We will now **select Amine Generating Groups** from the menu.



Select: -NO₂ by **highlighting** the group and **clicking** the mouse button or pressing

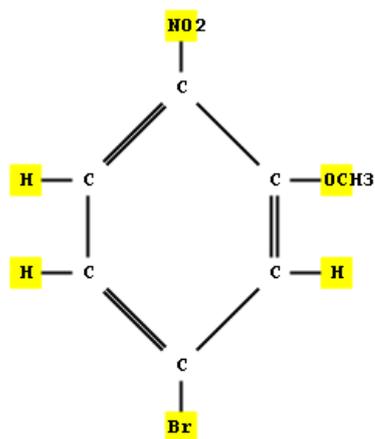


Highlight the appropriate atom and **click** the mouse button.



Select: Other.

Highlight -Br and click the left mouse button in order to place the substituent onto structure.

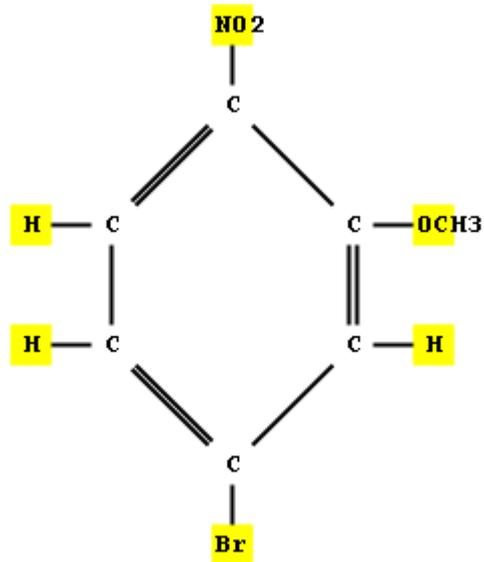


Now Press “Done” Button

At this point, the evaluation will be complete, and the justification report displayed.

Justification Report

OncoLogic Justification Report



SUMMARY :
CODE NUMBER : Aminel
SUBSTANCE ID : Aromatic amine #1

The level of carcinogenicity concern for this compound is
HIGH-MODERATE

JUSTIFICATION:

In general, the level of carcinogenicity concern of an aromatic amine

Press <Page Down> key to scroll through text.

is determined by considering the number of rings, the presence or absence of heteroatoms in the rings; the number and position of amino groups; the nature, number and position of other nitrogen-containing 'amine-generating groups'; and the type, number and position of additional substituents. Aromatic amine compounds are expected to be metabolized to N-hydroxylated/N-acetylated derivatives which are subject to further bioactivation, producing electrophilic reactive intermediates that are capable of interaction with cellular nucleophiles (such as DNA) to initiate carcinogenesis.

Nitro groups of aryl compounds can be reduced by nitro reductase to amino groups yielding aromatic amine compounds. The evaluation of this compound proceeds as if the nitro group were a free amine group.

An aromatic compound containing one benzene ring, one amino group, and one methyl or methoxy group ortho- to the amino group, has a carcinogenicity concern of HIGH-MODERATE.

The additional chloro and/or bromo group(s) generally raise(s) the level of concern, but they also impose an upper limit of HIGH-MODERATE on the concern level of the compound. Therefore, the level of concern remains HIGH-MODERATE.

The final level of carcinogenicity concern for this compound is HIGH-MODERATE.

Press <Close> key to return to main menu.