QSAR Toolbox

Customized search (Query Tool)

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Outlook

• What is Query Tool?
• Environmental fate - examples (BCF, BOD)
• Human health hazard - examples (AMES and Carcinogenicity)
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- What is Query Tool?
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Customized search (Query Tool)

What is Customized search?

Goal:

Searching for chemicals by applying different criteria such as:

- chemical identifiers,
- sub fragments,
- phys-chem properties,
- experimental data,
- profilers
Customized search (Query Tool)

Types customized search?

- Chemical identifier
  - CAS
  - Name

- Data
  - Experimental data accompanying with(out) metadata

- Parameter
  - 2D parameters
  - 3D parameters

- Extended
  - Profiling
  - Substructure
  - Similarity
Outlook

• What is Query Tool?
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• Human health hazard - examples (AMES and Carcinogenicity)
Example 1:

Biodegradable chemicals which are not bioaccumulative
(BOD $>60\%$ and BCF $\leq 2000$ L/kg wet)
Example 1: Biodegradable chemicals which are not bioaccumulative (BOD >60% and BCF ≤ 2000 L/kg wet)

Procedure of defining queries:
- Selection of databases
  - Bioaccumulation Canada
  - BCF fish CEFIC LRI
  - Bioconcentration NITE
  - Biodegradation NITE
**Example 1**: Biodegradable chemicals which are not bioaccumulative (BOD >60% and BCF ≤ 2000 L/kg wet)

Procedure of defining queries:
- Selection of databases
- Defining queries:
  - Endpoint: **BCF**
  - Species: *C. carpio*
  - Duration: 42 ÷ 56 days
  - Data: BCF < 2000 L/kg wet
Customized search (Query Tool)

Environmental search examples (BOD and BCF)

**Example 1**: Biodegradable chemicals which are not bioaccumulative (BOD >60% and BCF ≤ 2000 L/kg wet)

Procedure of defining queries:
- Selection of databases
- Defining queries:
  - Endpoint: BCF
  - Species: *C. carpio*
  - Duration: 42 ÷ 56 days
  - Data: BCF < 2000 L/kg wet
Customized search (Query Tool)

Environmental search examples (BOD and BCF)

**Example 1**: Biodegradable chemicals which are not bioaccumulative (BOD > 60% and BCF ≤ 2000 L/kg wet)

Procedure of defining queries:
- Selection of databases
- Defining queries:
  - Endpoint: **BCF**
  - Species: *C. carpio*
  - Duration: 42 ÷ 56 days
  - Data: BCF < 2000 L/kg wet
Customized search (Query Tool)
Environmental search examples (BOD and BCF)

**Example 1**: Biodegradable chemicals which are not bioaccumulative (BOD >60% and BCF ≤ 2000 L/kg wet)

Procedure of defining queries:
- Selection of databases
- Defining queries:
  - Endpoint: **BOD**
  - Guideline: OECD 301C
  - Data: BOD > 60%
Customized search (Query Tool)  
*Environmental search examples (BOD and BCF)*

**Example 1:** Biodegradable chemicals which are not bioaccumulative (BOD > 60% and BCF ≤ 2000 L/kg wet)

Procedure of defining queries:
- Selection of databases
- Defining queries:
  - Endpoint: **BOD**
  - Guideline: OECD 301C
  - Data: BOD > 60%
**Customized search (Query Tool)**

*Environmental search examples (BOD and BCF)*

**Example 1:** Biodegradable chemicals which are not bioaccumulative (BOD > 60% and BCF ≤ 2000 L/kg wet)

Procedure of defining queries:
- Selection of databases
- Defining queries
- Combining queries by logical operator

Queries are logically AND-ed

Possibility to execute separate query and logical combination

Save and load the defined query
Customized search (Query Tool)
Environmental search examples (BOD and BCF)

**Example 1:** Biodegradable chemicals which are not bioaccumulative (BOD >60% and BCF ≤ 2000 L/kg wet)

**Results:** 5 chemicals meeting the criteria of the defined queries
Customized search (Query Tool)
Environmental search examples (BOD and BCF)

Example 2:

Correspondence between lipophilicity and bioaccumulation (BCF). Not all lipophilic chemicals are bioaccumulative.

Query: lipophilic (log $K_{ow}>4.2$) and not bioacumulative chemicals (BCF<1000 L/kg wet)
**Customized search (Query Tool)**

*Environmental search examples (BOD and BCF)*

**Example 2:** Query is \( \log K_{ow} > 4.2 \) and not bioacumulative data (BCF < 1000 L/kg wet)

Procedure of defining queries:
- Selection of databases
  - Bioaccumulation Canada
  - BCF fish CEFIC LRI
  - Bioconcentration NITE
  - Biodegradation NITE

Selection of databases with BCF and BOD data
Customized search (Query Tool)
Environmental search examples (BOD and BCF)

Example 2: Query is $\log K_{ow} > 4.2$ and not bioaccumulative data (BCF < 1000 L/kg wet)

Procedure of defining queries:
- Selection of databases
- Defining queries:
  - Endpoint: BCF
  - Species: C.carpio
  - Duration: 42 ÷ 56 days
  - Data: BCF < 1000 L/kg wet
Customized search (Query Tool)
Environmental search examples (BOD and BCF)

**Example 2:** Query is \( \log Kow > 4.2 \) and not bioaccumulative data (BCF < 1000 L/kg wet)

Procedure of defining queries:
- Selection of databases
- Defining queries:
  - 2D parameters: \( \log Kow \) > 4.2
  - Threshold: \( \log Kow > 4.2 \)
Customized search (Query Tool)
Environmental search examples (BOD and BCF)

**Example 2**: Query is log $K_{ow} > 4.2$ and not bioaccumulative data ($BCF < 1000$ L/kg wet)

Procedure of defining queries:
- Selection of databases
- Defining queries:
  - Combining queries by logical operator

Queries are logically AND-ed
Customized search (Query Tool)
Environmental search examples (BOD and BCF)

**Example 2:** Query is $\log Kow > 4.2$ and not bioacumulative data ($BCF < 1000 \text{ L/kg wet}$)

**Results:** 151 chemicals meeting the criteria of the defined queries
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*Human health hazard examples (AMES, Carcinogenicity)*

**Example:**

Mutagenic chemicals (AMES positive) which are not carcinogenic
Customized search (Query Tool)

Human health hazard examples (AMES, Carcinogenicity)

**Example**: Mutagenic chemicals (AMES positive) which are not carcinogenic

Procedure of defining queries:
- Selection of databases
  - Carcinogenicity potency DB CPDB
  - Carcinogenicity & mutagenicity ISSCAN
  - Bacterial ISSTY
  - Genotoxicity OASIS
  - Toxicity Japan

Selection of databases with Carcinogenicity and AMES data
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*Human health hazard examples (AMES, Carcinogenicity)*

**Example:** Mutagenic chemicals (AMES positive) which are not carcinogenic

Procedure of defining queries:
- Selection of databases
- Defining queries:
  - **AMES positive**
    - Endpoint: Gene mutation
    - Test type: Bacterial reverse mutation assay (e.g. Ames)
    - Type of method: In vitro
    - Species: *S. typhimurium*
    - Metabolism: with S9
    - Scale: Gene mutation I
    - Data: Positive
**Customized search (Query Tool)**

*Human health hazard examples (AMES, Carcinogenicity)*

**Example**: Mutagenic chemicals (AMES positive) which are not carcinogenic

Procedure of defining queries:
- Selection of databases
- Defining queries:
  - **AMES positive**
    - Endpoint: Gene mutation
    - Test type: Bacterial reverse mutation assay (e.g. Ames)
    - Type of method: In vitro
    - Species: *S. typhimurium*
    - Metabolism: *with S9*
    - Scale: Gene mutation I
    - Data: Positive
  - Define restrictive condition

Queries associated with negative and equivocal data

Define restrictions: search for chemicals with positive data only. Chemicals with negative and equivocal data are excluded from query (shown on next slide)
Queries defining negative and equivocal data are logically OR-ed and then negated (excluding from search).

Example: Mutagenic chemicals (AMES positive) which are not carcinogenic.

Procedure of defining queries:
- Selection of databases
- Defining queries:
  - AMES positive
    - Endpoint: Gene mutation
    - Test type: Bacterial reverse mutation assay (e.g. Ames)
    - Type of method: In vitro
    - Species: S. typhimurium
    - Metabolism: with S9
    - Scale: Gene mutation I
    - Data: Positive
    - Negating queries
Customized search (Query Tool)

*Human health hazard examples (AMES, Carcinogenicity)*

**Example:** Mutagenic chemicals (AMES positive) which are not carcinogenic

Procedure of defining queries:
- Selection of databases
- Defining queries:
  - **AMES positive**
  - Endpoint: Gene mutation
  - Test type: Bacterial reverse mutation assay (e.g. Ames)
  - Type of method: In vitro
  - Species: *S. typhimurium*
  - Metabolism: *with S9*
  - Scale: Gene mutation I
  - Data: Positive
  - Negating queries

Combining queries by logical operator **AND**
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*Human health hazard examples (AMES, Carcinogenicity)*

**Example:** Mutagenic chemicals (AMES positive) which are not carcinogenic

Procedure of defining queries:
- Selection of databases
- Defining queries:
  - **Carcinogenic negative**
    - Endpoint: Summary carcinogenicity
    - Species: *rat*
    - Scale: Carcinogenicity I (ISSCAN)
    - Data: Negative

![Diagram showing query definition process](image)
Customized search (Query Tool)

*Human health hazard examples (AMES, Carcinogenicity)*

**Example:** Mutagenic chemicals (AMES positive) which are not carcinogenic

Procedure of defining queries:
- Selection of databases
- Defining queries:
  - **Carcinogenic negative**
    - Endpoint: Summary carcinogenicity
    - Species: *rat*
    - Scale: Carcinogenicity (ISSCAN)
    - Data: Negative
    - Excluding positive and equivocal chemicals
Customized search (Query Tool)

*Human health hazard examples (AMES, Carcinogenicity)*

**Example:** Mutagenic chemicals (AMES positive) which are not carcinogenic

Procedure of defining queries:
- Selection of databases
- Defining queries
- Combining queries
  - Ames positive
  - Carcinogenic negative
Customized search (Query Tool)

Human health hazard examples (AMES, Carcinogenicity)

Example: Mutagenic chemicals (AMES positive) which are not carcinogenic

Results: 12 chemicals meeting the searched criteria