




Searching information on alternatives to animal testing: good practice

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## Searching for alternative or 3Rs methods

= mandatory step before starting experimental protocol

Why ?

- legal obligation
  - European Directive 2010/63/EU : «...live animals may only be used if the specific scientific goals pursued cannot be achieved by any other means... »
- need scientific evidence to perform a high quality experimental

## Initiatives for increasing validity and reliability

- CAMARADES (Collaborative Approach to Meta-Analysis and Review of Animal Data from Experimental Studies)
- NC3RS (National Centre for the 3Rs)
- ...
- PREPARE guidelines (*Planning Research and Experimental Procedures on Animals: Recommendations for Excellence*)



**Table 1.** The PREPARE guidelines short checklist.

| Topic                               |
|-------------------------------------|
| <b>(A) Formulation of the study</b> |
| 1. Literature searches              |

Smith et al., 2018

## Obstacles for performing information search



- Broad array of journals and sources
- Relevance of information
- Lack of information literacy skills
- Time-consuming
- ...

## Developing a 3Rs search strategy and searching for evidence

step by step



1. Clearly define your specific need
2. Start your search
  - in 3Rs specific context : databases or websites
  - in bibliographic databases
3. Evaluate the results and refine the search strategies if necessary



ECVAM Search Guide


 European Centre for  
the Validation of  
Alternative Methods

Available for free  
<https://ec.europa.eu/jrc/en/scientific-tool/eurl-ecvam-search-guide>

## Step 1

### Designing the search strategy

### Clearly define your specific information need



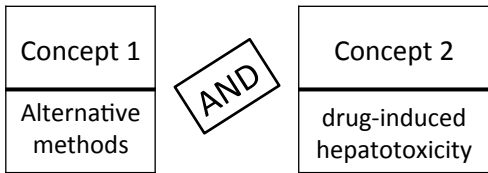
Formulate the question

Highlight the concepts  
(relevant search terms)



### Identify

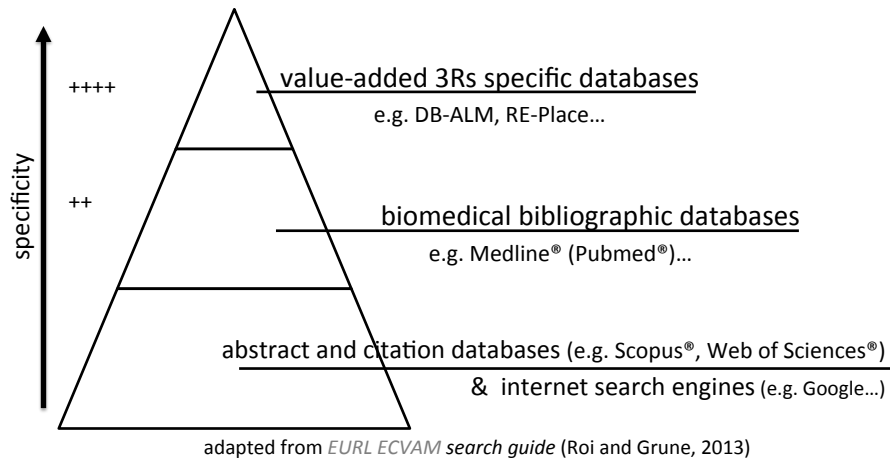
- ① concepts
- ② Boolean logic operators (AND, OR, NOT)



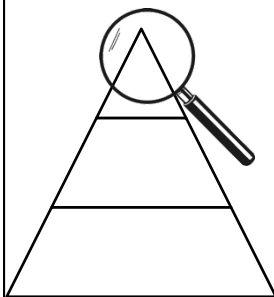
## Step 2

### Searching in appropriate information resources

## Available information resources



## Upper level: value-added 3Rs specific databases



- ECVAM

-> *alternatives to animal testing and safety assessment of chemicals*

<https://ec.europa.eu/jrc/en/eurl/ecvam>

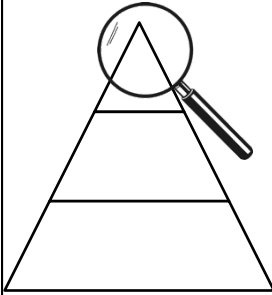
- ☑ DB-ALM : repository for alternative methods to animal experimentation

<https://ecvam-dbalm.jrc.ec.europa.eu/>

- ☑ TSAR : information on alternative methods submitted for validation in the context of the EU regulations on chemicals

<https://tsar.jrc.ec.europa.eu/>

## Upper level: value-added 3Rs specific databases



- RE-Place



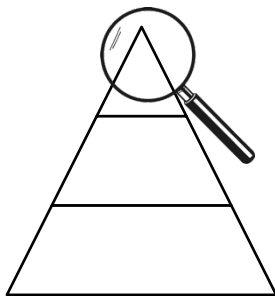
<https://www.re-place.be>

the Belgian platform that aims to collect all alternative methods to animal testing in one central database

- And many others

## Take home message

Your starting point = value-added 3Rs specific database



- number of available documents is easy to handle
- specific context
- some expert review
- easy to use and straightforward searching strategy

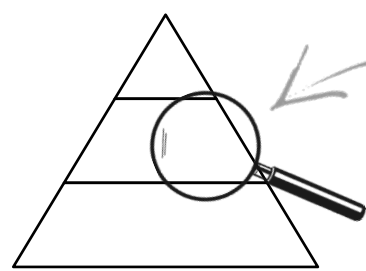
at this point after searching in the value-added 3Rs specific databases you already have...

Rodrigues et al. *Stem Cells Dev* 2014;23:44-55



Coll et al. *Cell Stem Cell* 2018;23:101-113

Middle level: biomedical bibliographic databases



bibliographic databases for each article indexed: title, abstracts and assigned keywords

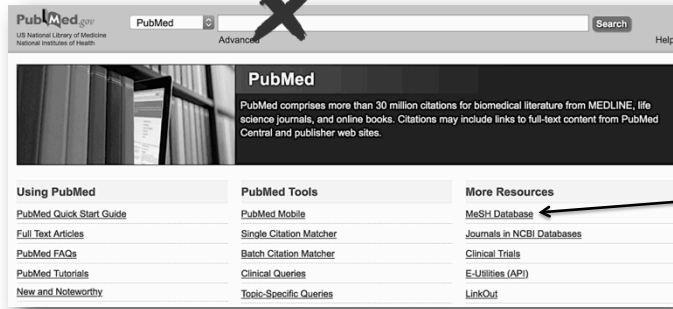
Need information (sept 2019) on bibliographic databases of interest: https://www.library.ucdavis.edu/guide/alternatives/



# Medline®

www.pubmed.gov

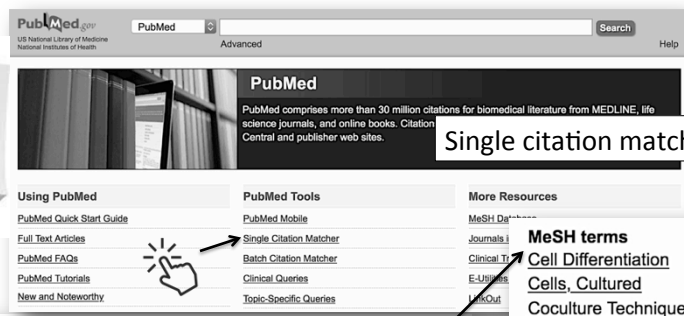
- Covers well ++ peer-reviewed journals publishing articles of interest in 3R
- Interface PubMed® : free of use



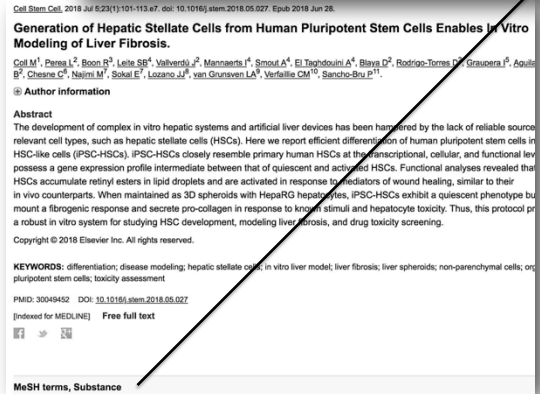
Use MeSH to search MEDLINE® / PubMed®



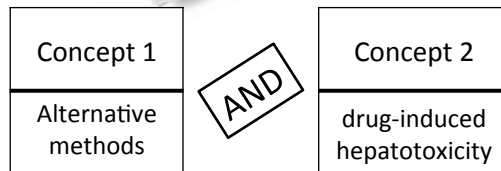
Searching PubMed® using MeSH search tags (PubMed® tutorials, on line)



Single citation matcher



- MeSH terms**
- Cell Differentiation
  - Cells, Cultured
  - Coculture Techniques
  - Female
  - Hepatic Stellate Cells/drug effects
  - Hepatic Stellate Cells/pathology\*
  - Humans
  - Infant, Newborn
  - Liver Cirrhosis/drug therapy
  - Liver Cirrhosis/pathology\*
  - Liver Cirrhosis/therapy\*
  - Male
  - Models, Biological\*
  - Pluripotent Stem Cells/cytology\*
  - Thioacetamide
  - Wound Healing



| Concepts                                 | MeSH terms  |
|--|---|
| drug-induced hepatotoxicity              | "Liver Cirrhosis"[Mesh] OR<br>(("Liver"[Mesh] OR "Hepatocytes"[Mesh]) AND "Toxicity Tests"[Mesh]) OR<br>(("Liver"[Mesh] OR "Hepatocytes"[Mesh]) AND "Toxicology"[Mesh]) OR<br>("Liver/drug effects"[Mesh] OR "Hepatocytes/drug effects"[Mesh]) OR<br>"Chemical and Drug Induced Liver Injury"[Mesh] |
| alternative methods                      | "Cells, Cultured"[Mesh] OR "Stem Cells"[Mesh] OR<br>"Models, Biological"[Mesh] OR "Animal Testing Alternatives"[Mesh]   |
| November 20, 2019 -> n citations = 29019 |   |

> a first evaluation is needed

### After an initial evaluation of the results

- Exclusion (if pertinent) : by using Boolean operator NOT

NOT ("Disease Models, Animal"[Mesh] OR "Liver Neoplasms"[Mesh] )

n citations = 19432

- Use filters like « publication date »

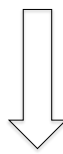
Filters activated: Publication date from 2010/01/01

n citations = 8705

PubMed® keeps your searches for 8 hours



  
**TIP**

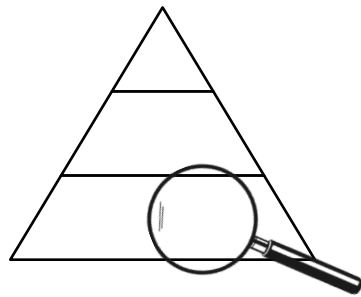


Save your PubMed® search queries

to modify your  
searches  
afterwards

to provide email  
automatic updates  
(alert) for saved  
searches

### Lower level: non specialized tools



abstract and citation databases  
(e.g. Scopus®, Web of Sciences®)  
&  
internet search engines (e.g. Google...)

Natural language

all synonyms  
for each concept

### Natural language

Concept  
liver

Synonyms  
liver  
hepatocyte(s)  
...  
hepatic

Related terms  
hepatotoxicity



Query : liver OR hepatocyte OR hepatocytes OR hepatic OR hepatotoxicity

## Food for thought...

- The quality of the search methodology will be decisive for the quality of the results
- Don't forget the pyramid
- Evaluate the results
- In your further publication, add the notion of 3Rs or alternatives to animal testing

## Your turn...





## To help you

Avey MT, Fenwick N, Griffin G. The use of systematic reviews and reporting guidelines to advance the implementation of the 3Rs. *J Am Assoc Lab Anim Sci* 2015;54(2):153-162.

European Chemicals Agency Practical guide; how to use alternatives to animal testing to fulfil your information requirements for REACH registration. 2016 [available online]

Smith AJ, Clutton RE, Lilley E, Hansen KEA, Brattelid T. PREPARE: guidelines for planning animal research and testing. *Lab Anim* 2018;52(2):135-141.