



# Tips from FIZ Search Service

## No 1- Don't be afraid of Markush

Miriam Kuhlmann

# Agenda

- What are Markush structures and why are they used in patents
- Markush structures and where to search them
- Example
- Key takeaways

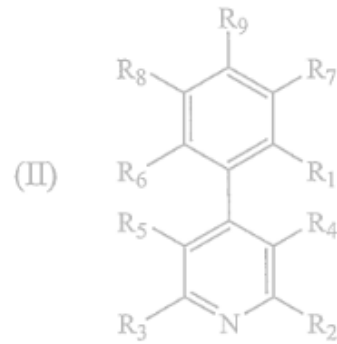
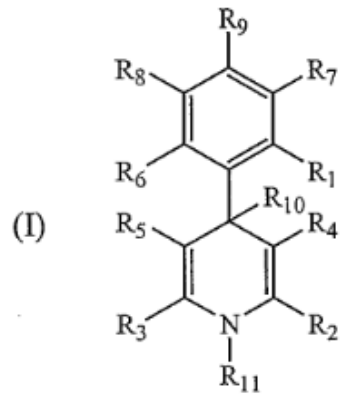


# What are Markush structures

## WO 2004/075893 A1

(54) Title: METHOD OF TREATMENT OF CARDIAC AND/OR RENAL FAILURE USING A CALCIUM CHANNEL BLOCKER AND AN ANGIOTENSIN CONVERTING ENZYME INHIBITOR OR AN ANGIOTENSIN II RECEPTOR BLOCKER

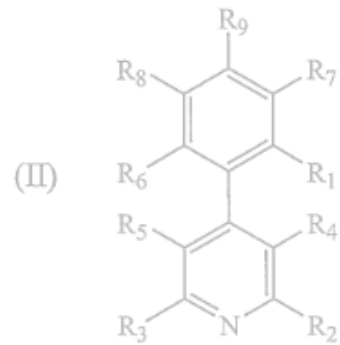
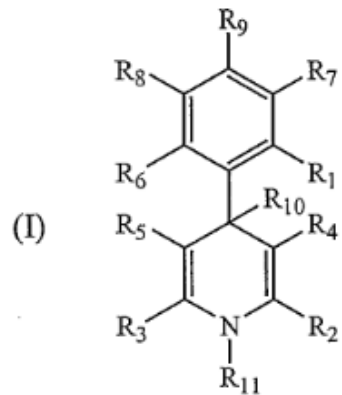
1. A pharmaceutical composition comprising an angiotensin converting enzyme (ACE) inhibitor and a calcium channel blocker (CCB), wherein said CCB is a compound of Formula I or II



# What are Markush structures

Markush structures are **generalized structural formulas** describing a group of structurally similar compounds.

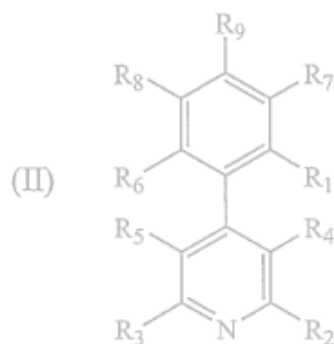
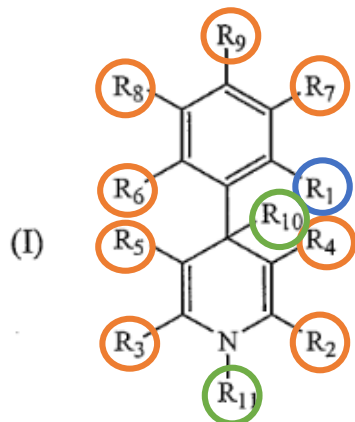
1. A pharmaceutical composition comprising an angiotensin converting enzyme (ACE) inhibitor and a calcium channel blocker (CCB), wherein said CCB is a compound of Formula I or II



# What are Markush structures

Markush structures are **generalized structural formulas** describing a group of structurally similar compounds.

1. A pharmaceutical composition comprising an angiotensin converting enzyme (ACE) inhibitor and a calcium channel blocker (CCB), wherein said CCB is a compound of Formula I or II



or a pharmaceutically acceptable salt, amide, ester, or prodrug thereof,

where

a)  $R_1$  is a straight-chain, branched, or cyclic alkyl group having greater than eight carbon atoms;

b)  $R_2$ - $R_9$  are each independently selected from the group consisting of hydrogen, halogen, perhaloalkyl, nitro, amino, a diazo salt, optionally substituted lower alkyl, optionally substituted lower alkylene, optionally

c)  $R_{10}$  and  $R_{11}$  in the compound of Formula I are each independently selected from the group consisting of hydrogen and lower alkyl.

mercaptyl, optionally substituted lower mercaptoalkyl, optionally substituted lower mercaptomercaptyl,  $-C(O)OH$ ,  $-OC(O)H$ ,  $-C(O)OR$ ,  $-OC(O)R$ ,  $-C(S)OR$ ,  $-OC(S)R$ ,  $-C(O)SR$ ,  $-SC(O)R$ ,  $-C(S)SR$ ,  $-SC(S)R$ , C-amido, N-amido, and optionally substituted five- or six-membered heteroaryl ring or optionally substituted six-membered aryl or heteroaryl ring,

where the lower alkyl and the lower alkylene moieties are each

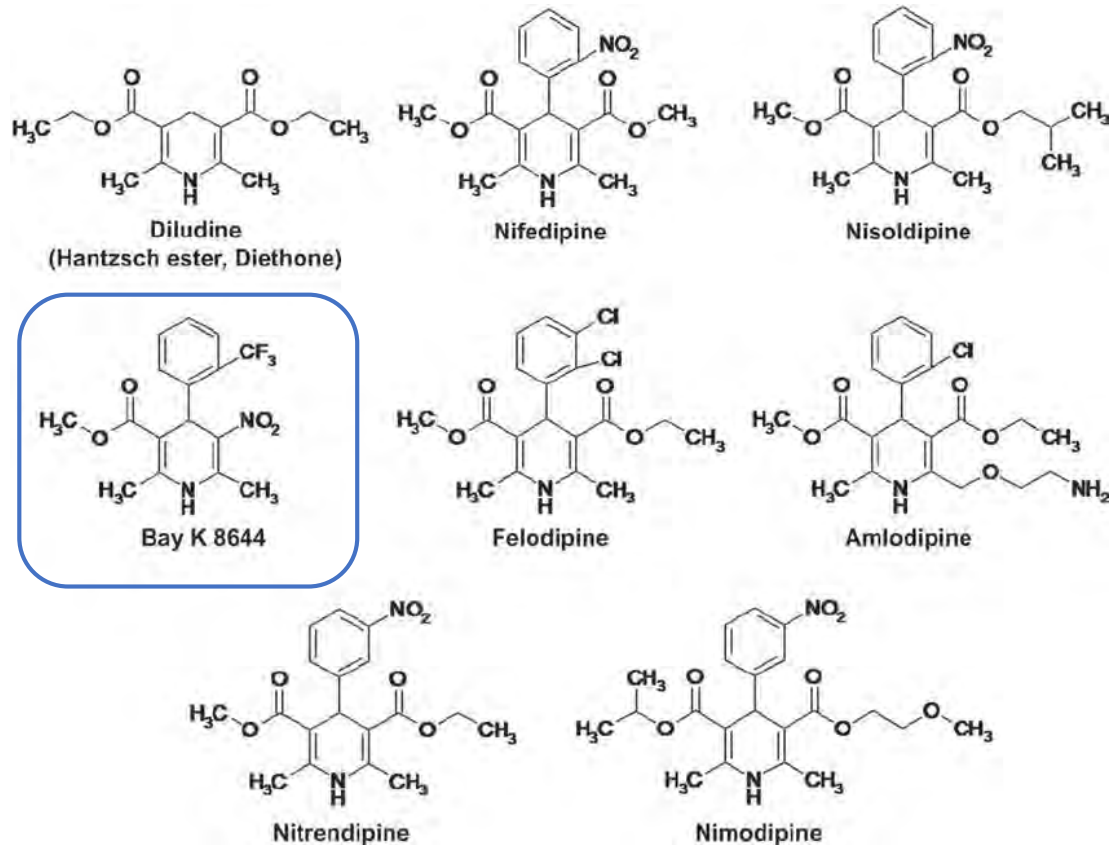
# Searching Markush structures – „why and where“?

- Why are Markush structures used?
  - One Markush structure can describe all of the invention-relevant substances
  - Not necessary to protect a multitude of possible specific structures separately
- Where are Markush structures used?
  - Especially in the fields of pharma and chemistry
- Why should they be searched?
  - Also a specific structure could be protected by a Markush patent
  - Markush searches are essential for comprehensive structure searches
- Where to search them?
  - Markush databases: MARPAT and DWPIM
  - STN offers highly customizable search in MARPAT and DWPIM
- Example following ...

MARPAT and DWPIM:  
Markush structures are  
intellectually indexed!

# Example

- Compound class of dihydropyridines – calcium channel inhibitors used against hypertension

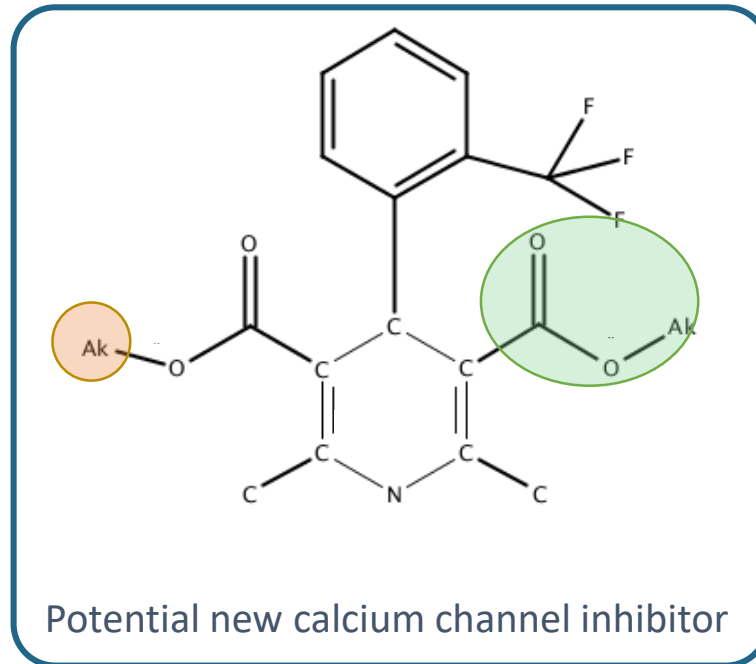
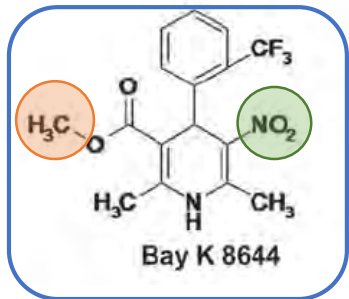


Imagine:

- A potentially new compounds of this class have been developed – e.g. derivatives of Bay K 8644

# Example

- Compound class of dihydropyridines – calcium channel inhibitors used against hypertension

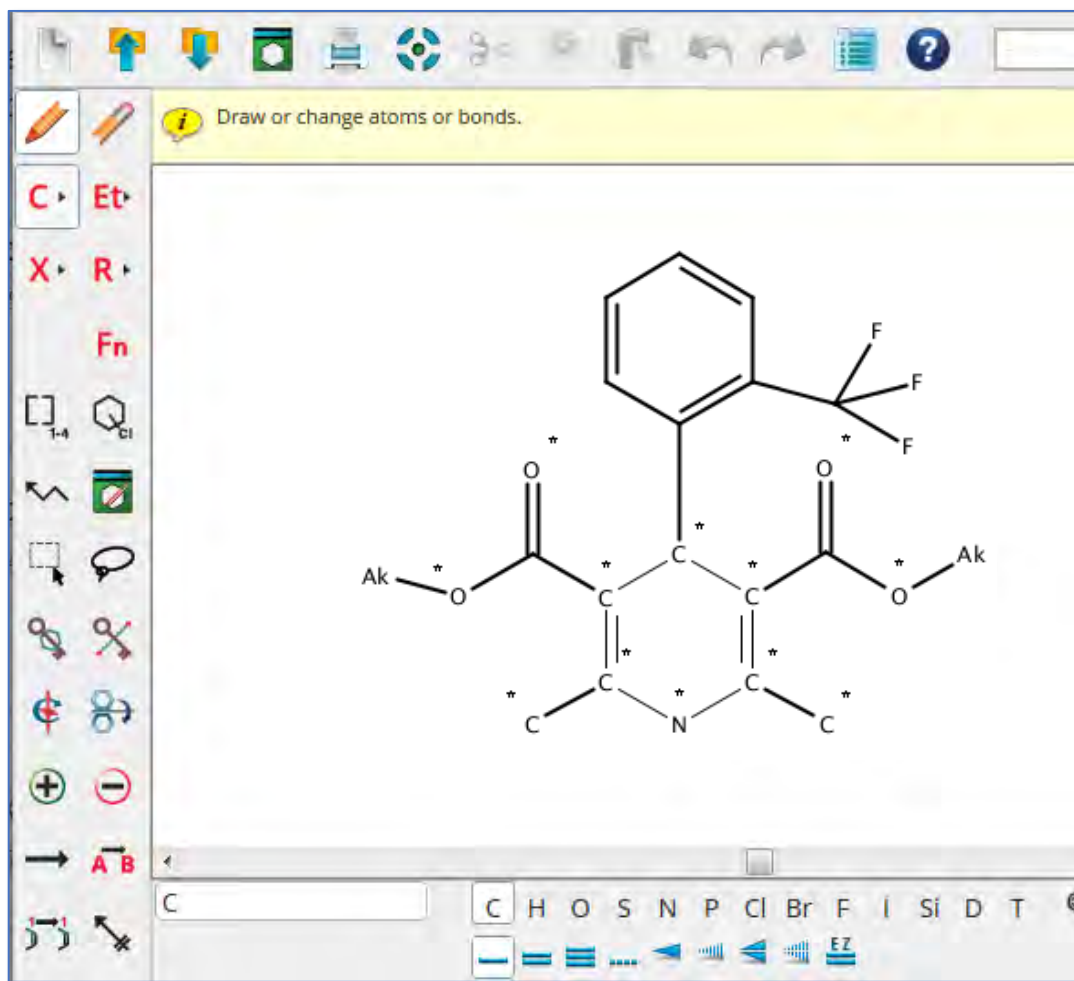


Imagine:

- A potentially new compounds of this class have been developed – e.g. derivatives of Bay K 8644
- It might be described by the following structure
  - The **nitro group** was changed to an **ester group**
  - The **methyl ester** might be any **alkyl ester**
- Are these derivatives really new? And are they protected by (Markush) patents?



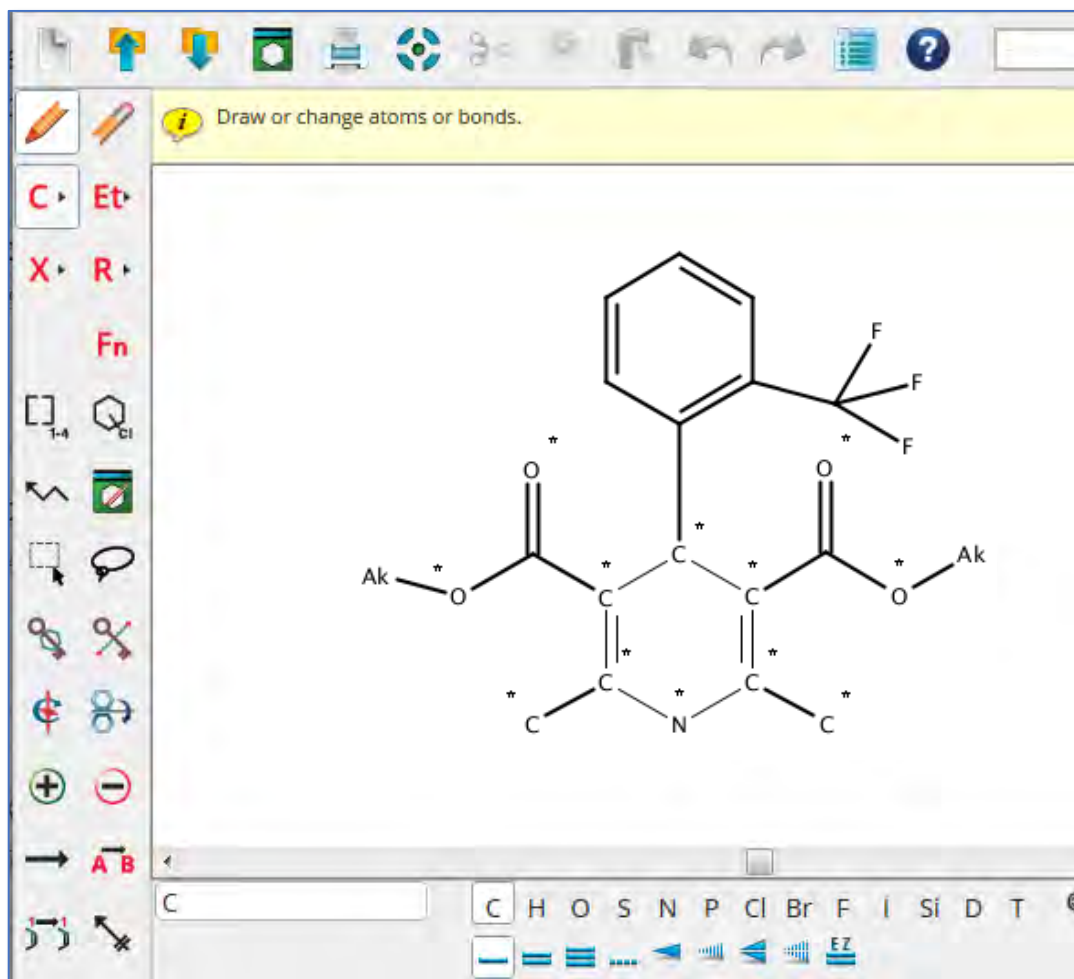
# Example – Structure search with STNext



- 1) Draw and define all necessary structure parts in STNext structure editor.

If you are not sure about the Markush search parameters, ask the Helpdesk.

# Example – Structure search with STNext



- 1) Draw and define all necessary structure parts in STNext structure editor
- 2) Perform structure search in REGISTRY to retrieve specific substances.  
→ Cross-over to get patent families (and NPL) in CAPLUS
- 3) Search in MARPAT and retrieve patents that meet your structure query.
- 4) Search in the chemical resource DCR of DWPI and get the patents including the substances.
- 5) Perform search in DWPIM.  
→ Cross-over to get patent families in DWPI

Duplicates can be removed by transferring and subtracting the patent numbers retrieved so far.

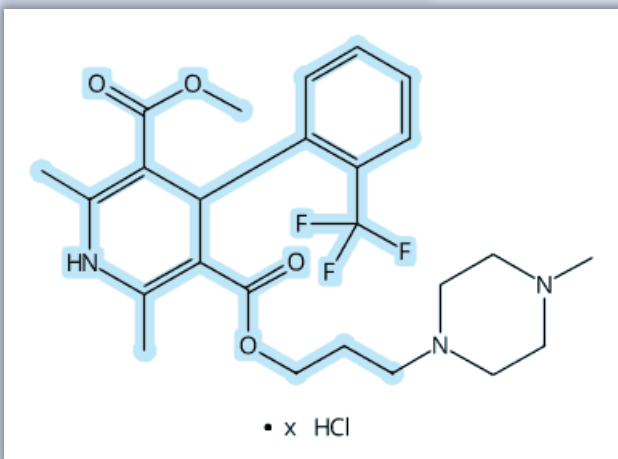
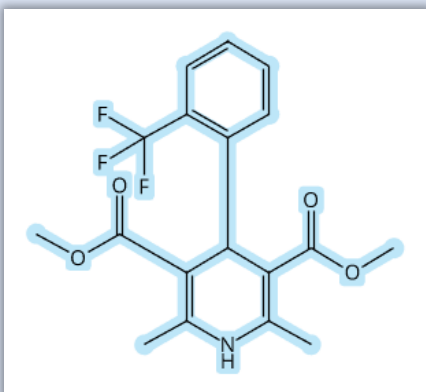
# Unique extra results from Markush searches

REGISTRY/CAPLUS	MARPAT	DCR/DWPI	DWPIM/DWPI
324 substances ↓		5 substances ↓	215 Markush structures ↓
141 Pat. (+ 207 NPL)	227 Pat.	17 Pat.	161 Pat.
	<b>164 additional</b> to REGISTRY/CAPLUS	<b>3 additional</b> to REGISTRY/CAPLUS, MARPAT	<b>22 additional</b> to REGISTRY/CAPLUS, MARPAT, DCR

Markush databases  
retrieve unique  
extra results!

# Example Results

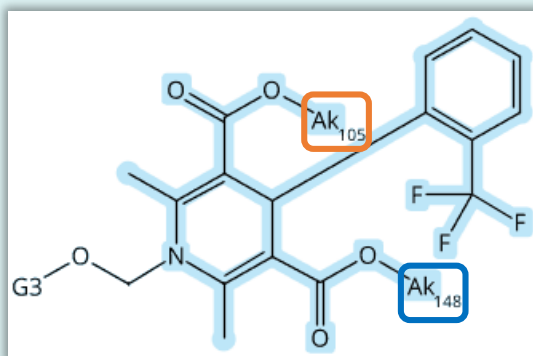
## REGISTRY/CAPLUS (Substance based)



## MARPAT extra results (MARKUSH based)

TI Process for the preparation of 1-(alkoxymethyl)-1,4-dihydro-3-pyridinecarboxylic acids by selective saponification of dialkyl 1-(alkoxymethyl)-1,4-dihydro-3,5-pyridinedicarboxylates (e.g., nifedipine analogs)

### MSTR 2 Assembled



**105:** alkyl <containing 1-4 C>

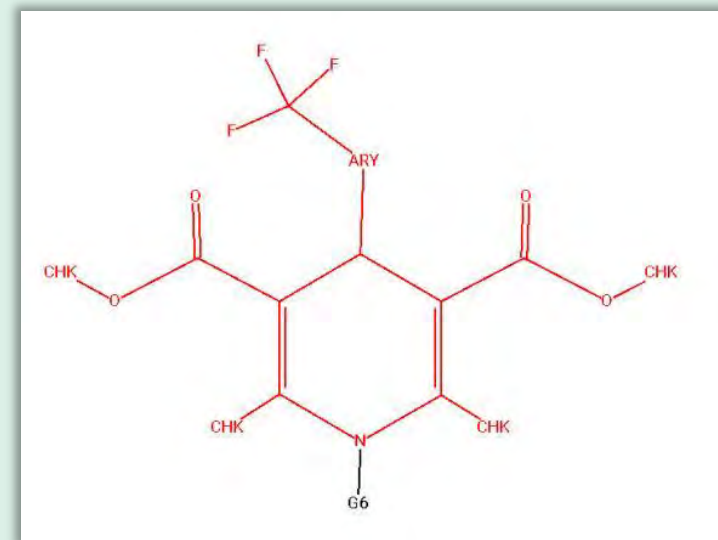
**148:** alkyl <containing 1-4 C>

Patent location:

claim 1

## DWPIM / DWPI extra results (MARKUSH based)

TI New 1,4-dihydro:pyridine derivs. - active against drug-resistant tumour cells by inhibiting excretion of chemotherapeutic agents from tumour cells



CHK: Hydrocarbon chain

ARY: Aryl

# Key takeaways

- Substance databases **REGISTRY** and **Derwent Chemical Resource (DCR)** do **not include** any structures from **Markush patents**
  - A substructure search in REGISTRY or DCR – even if it looks like a Markush structure (e.g. with variables like Ak) – cannot retrieve a substance claimed by a Markush structure
- Some highly relevant structures may be disclosed by Markush structures!

For any questions concerning Markush structure searching contact the Helpdesk.

Or you can also assign structure searches to the FIZ Search Service.





# FIZ Search Service Team



- Scientists with several years of search experience
- We offer all kinds of patent and literature searches on STN
- Structure searches in REGISTRY/CAPLUS, MARPAT, DCR/DWPI and DWPIM/DWPI

Thank you for your attention  
and have a nice day!

 **FIZ Search Service**

FIZ Karlsruhe – Leibniz Institute for Information Infrastructure

# Contact Us



**FIZ Karlsruhe**

**[helpdesk@fiz-karlsruhe.de](mailto:helpdesk@fiz-karlsruhe.de)**  
**[www.stn-international.de](http://www.stn-international.de)**

**CAS**

**[help@cas.org](mailto:help@cas.org)**  
**[www.cas.org](http://www.cas.org)**

**FIZ Search Service**

**[search.service@fiz-karlsruhe.de](mailto:search.service@fiz-karlsruhe.de)**  
**[www.fiz-karlsruhe.de/en/search-service.html](http://www.fiz-karlsruhe.de/en/search-service.html)**