



**JKI**

**Julius Kühn-Institut**

Bundesforschungsinstitut für Kulturpflanzen  
Federal Research Centre for Cultivated Plants

**CADIMA:**

An open-access online tool and database increasing the transparency and facilitating the synthesis of (GMO) impact data

Christian Kohl

8<sup>th</sup> MEACB, Liège, 24. November 2017

[www.julius-kuehn.de](http://www.julius-kuehn.de)

# The Julius Kühn-Institut...



➔ ... is the **Federal Research Centre for Cultivated Plants** in Germany

➔ ... is both a research institute and a higher federal authority.



Major research areas are:

- plant genetics, breeding research
- plant nutrition, agronomy and soil science
- plant protection and plant health

# Organization



➔ 17 specialized institutes

➔ **Institute for Biosafety in Plant Biotechnology**

Impact assessment (risks and benefits) of plant biotechnology – including genetic engineering and new plant breeding techniques

➔ **CADIMA**

Developed in the course of the EU-funded project GRACE

Two major areas:

- Information hub for impact assessment of crop genetic improvement technologies
- Open access online tool supporting the conduct and reporting of systematic reviews

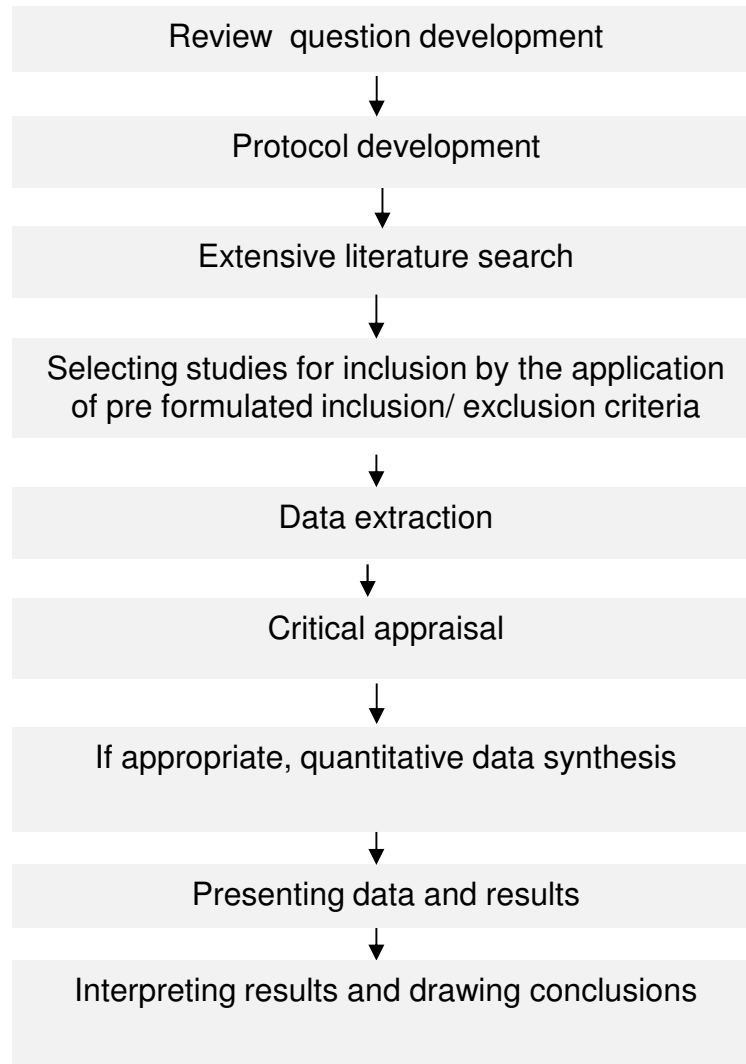
Permanently maintained and further developed by JKI

# The systematic review concept



- Systematic review is a structured, reproducible, and rigorous approach for answering a specific question
  
- Provides a defensible answer to a specific question by:
  - Increasing precision by the performance of a quantitative data synthesis (if feasible)
  
  - Minimizing bias by following a standardized procedure comprising so called “core” steps

# Core steps of a systematic review



**Document what you did and why you did it!**

# Review question development



Does the growing of Bt maize change populations or ecological functions of non-target arthropods compared to the growing of conventional non-GM maize?

P = population

I = intervention

C = comparator

O = outcome

# Protocol development

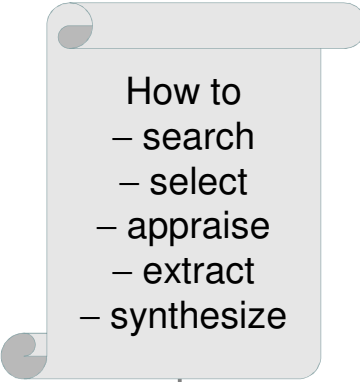


How to

- search
- select
- appraise
- extract
- synthesize

- It reduces bias by preventing deviation from planned methods
- It ensures transparency and repeatability of the methods
- Allows for active stakeholder involvement
- Should be peer reviewed

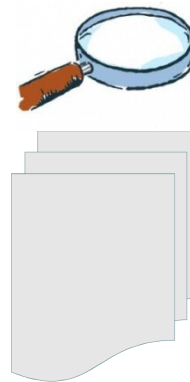
# Literature search

- 
- How to
  - search
  - select
  - appraise
  - extract
  - synthesize

(maize OR corn OR “Zea mays”) AND (transgenic OR Bt OR “Bacillus thuringiensis” OR GM OR “genetically modified” OR “genetically engineered” OR “Cry\*” OR “Vip\*”) AND (“non-target” or “nontarget” or “natural enemy” or predator or parasitoid or decomposer or pollinator)

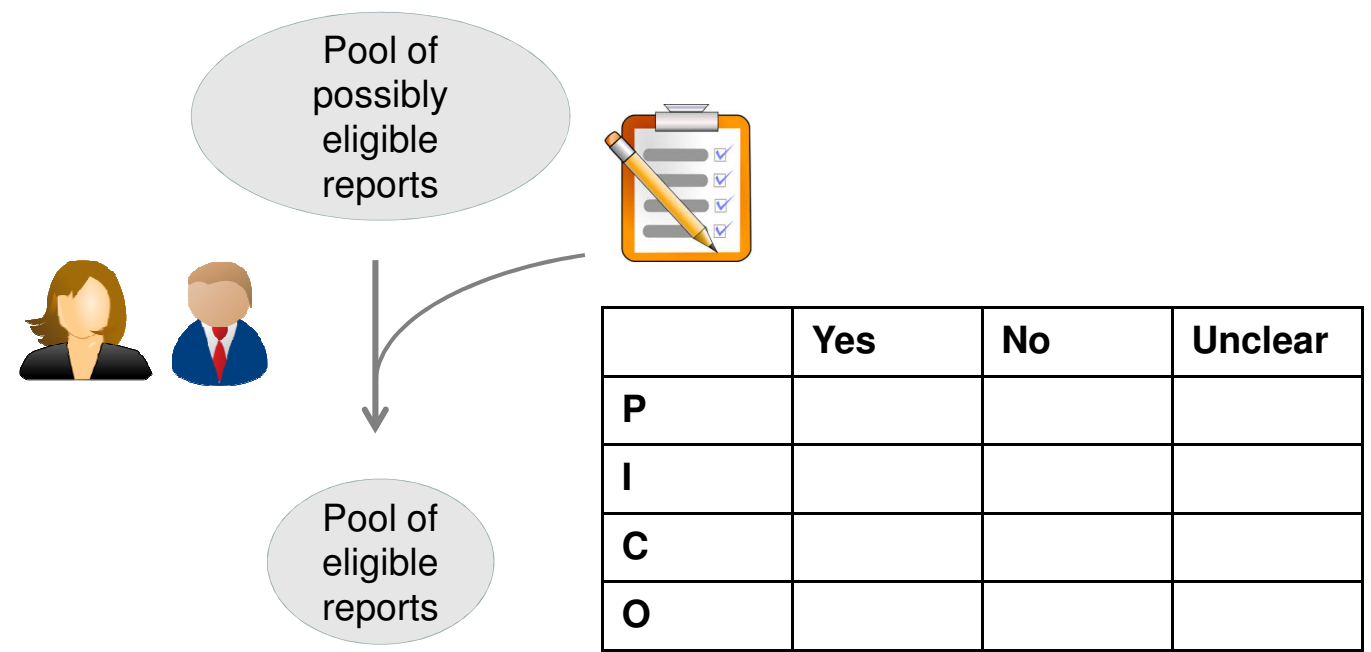
## Identification of the entire evidence base

- Comprehensive
  - Should include an adequate range of relevant information sources
- Grey literature
  - Organizational websites
  - Stakeholder contacts
  - Databases of theses

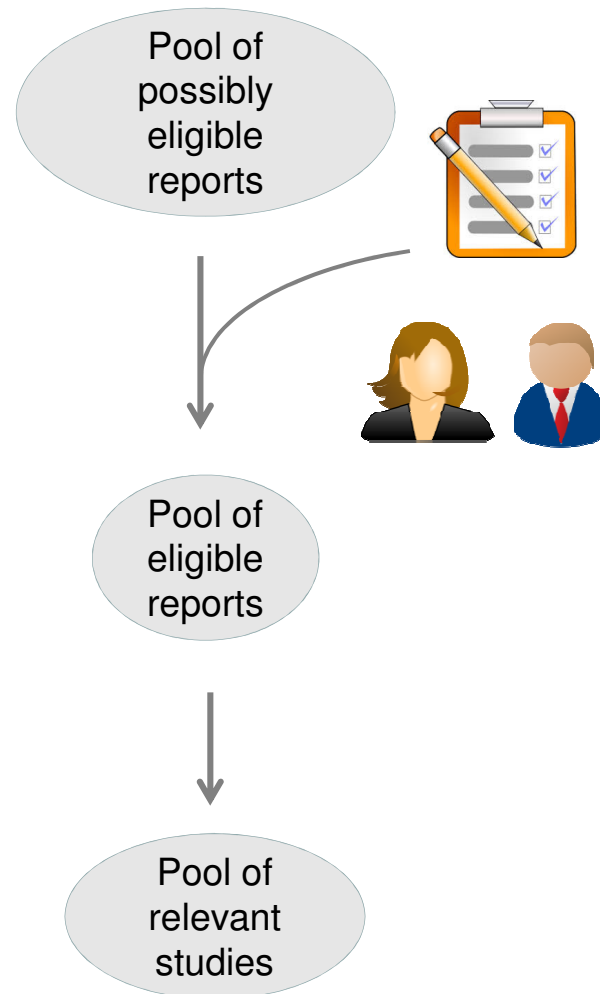




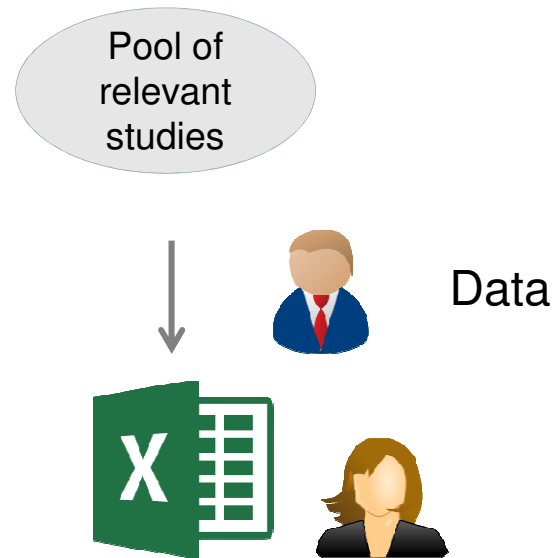
# Study selection



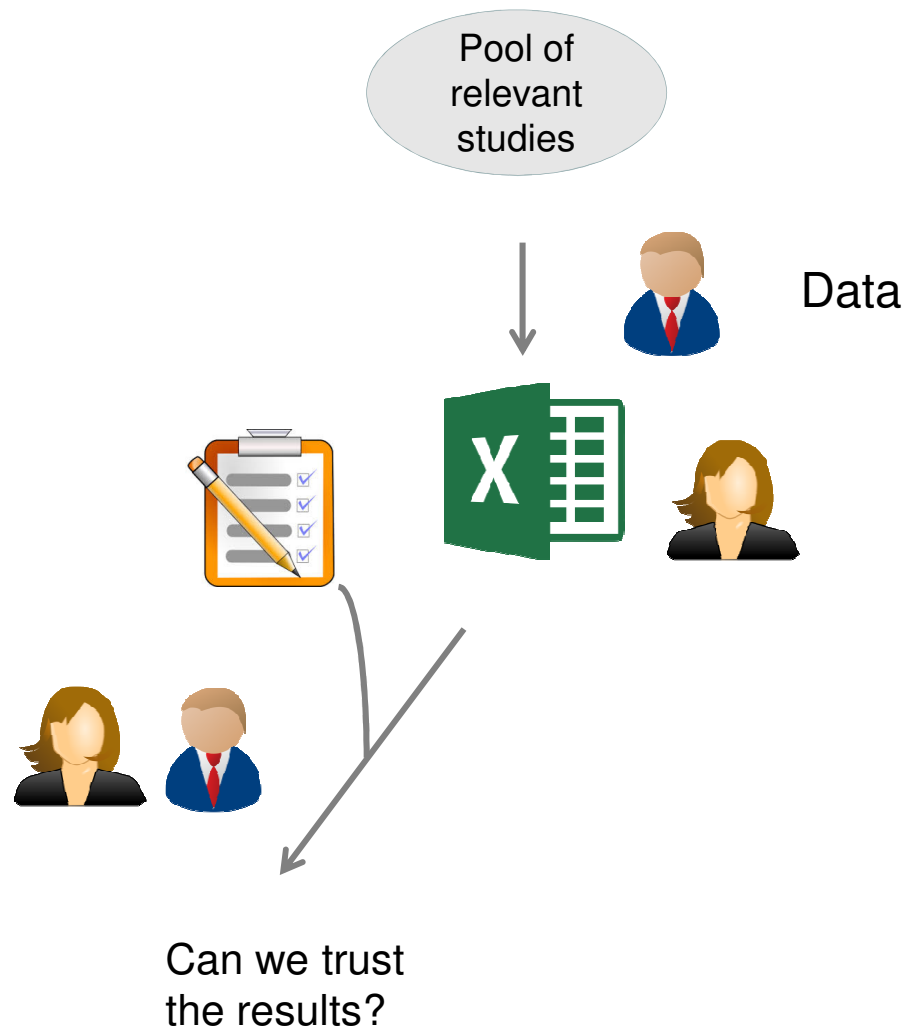
# Study selection



# Data extraction



# Critical appraisal

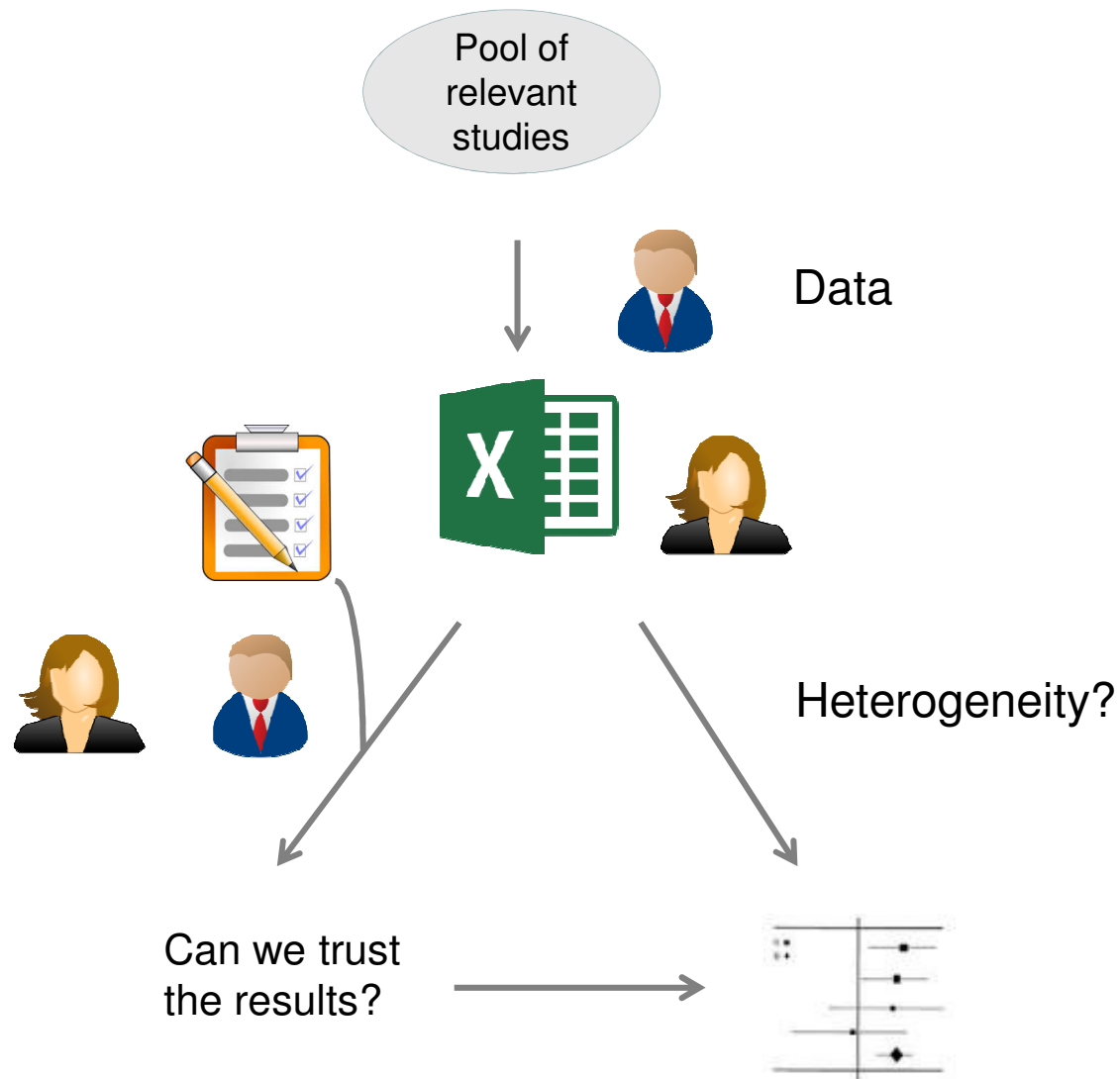


# Critical appraisal



- Including biased studies in the data synthesis step of a systematic review will cause the results of the review to be biased
  
- How much do I trust the results?
  - Internal validity
  
- How generalisable are the study results?
  - External applicability

# Critical appraisal and synthesis



# Limitations



- Sufficient and robust primary research data would have to be available for a systematic review to provide useful information
  - Systematic reviews do not provide an immediate answer to a question
  - Systematic reviews can be resource intensive and are thus not always feasible
    - Online tools can help to increase the efficiency of the evidence synthesis process
- => CADIMA

# CADIMA

The open-access database CADIMA is a non-profit internet portal provided and maintained by the Julius Kühn-Institut aiming to increase the transparency and traceability of information in agricultural and environmental sciences. To further explore the functions of CADIMA, please check out the area of your interest by clicking on the respective boxes below

## Evidence Synthesis Tool and Database

CADIMA supports the conduct of systematic reviews and evidence/systematic maps by the provision of a freely available online tool that:

1. guides review authors through the evidence synthesis process,
2. facilitates the coordination of cooperating team members,
3. eases steps with considerable workload and
4. guarantees for its thorough documentation

The evidence synthesis tool was established and is further developed in a close collaboration between the Julius Kühn-Institut and the Collaboration for Environmental Evidence

[>> click here <<](#)

## Information hub for impact assessment of crop genetic improvement technologies

CADIMA offers information services providing

1. a comprehensive overview and links to providers of information regarding the impact assessment of GMOs (Central Access Point)
2. open access to raw data from animal feeding trials with whole GM food/feed and alternative approaches generated during associated research activities (Animal Feeding Trials).
3. services related to specific projects: PreSto GMO-ERA-Net (partly restricted access)

[>> click here <<](#)



- Settings ✓
- Protocol ▾
- Literature search ▾
- Study selection ▾
- Data extraction ▾
- Critical appraisal
- Data synthesis
- Presenting data/results



Menu structure mirrors the core steps of a systematic review

## Settings

Title \* kappa

Evidence Synthesis Approach

Systematic Review  Evidence Map

Question Type

P I E C O

Team Member

### Available Users

<Select User>

+ add user

### Member of this evidence synthesis

Christian Kohl (Coordinator)  
[Change Coordinator...](#) ↻

Stefan Unger ×

Wilhelm Ralf

- Home
- Settings
- Protocol ▾
- Literature search ▾
- Define search string(s)
- Display merged reference list
- Study selection ▾
- Data extraction ▾
- Critical appraisal
- Data synthesis
- Presenting data/results

## Define search string(s)

- Please enter the developed search strings and the databases (or further sources) they were applied to by clicking on "create new search string". In a next step, please upload (↑) for each search string and database the retrieved reference list as RIS file. CADIMA will automatically calculate the number of imported references.
- Please check that all abstracts are entered for each reference by clicking on view reference list (📄), displaying the details for each reference by clicking on (🔍).
- When all database searches are filed in, please proceed with "display merged reference list"

➕ Create new search string




Total 1 result.

Select	🗑️	✍️	↑	📄	↓	↓	➡️	Search string	Database source	#results (#origin)	Date
<input type="checkbox"/>	🗑️	✍️		📄	↓(10000)	↓(10000)	➡️	(maize OR corn OR "Zea mays") AND (field* OR plot* OR location* OR trial* OR farm-scale OR scouting OR trap* OR sampl* OR monitor*) AND (transgenic OR Bt OR "Bacillus thuringiensis" OR GM OR "genetically modified" OR "genetically engineered" OR "Cry*" OR "Vip*") AND ("non-target" or "nontarget" or "natural enemy" or predator or parasitoid or decomposer or pollinator)	Scopus	10000 (10000)	2017-09-04

➡️ Display merged reference list

CADIMA vers. 1.7.5 - Aug 2017  
Copyright © 2012 - 2017

✉️ [Leave a comment](#)

Supported by  GRACE and  PreSto ERA-Net and  G-TWYST  
JKI - Julius Kühn-Institut - Federal Research Centre for Cultivated Plants  
Implementation: Stefan Unger, Robin Kluth, Toni Schreiber, Steffen Kecke  
Design: Stefan Unger, Anja Wolck, Christian Kohl, Neal Haddaway, Steffen Kecke  
Scientific support: Christian Kohl, Neal Haddaway, Ralf Wilhelm



- No search engine but reference lists can be exchanged e.g. with Endnote as RIS files
  - Upload of 10000 entries ~ 3 min
- Duplicates are recognized but currently no automated duplicate removal possible
  - Included in version 2.0

- Home
- Settings ✓
- Protocol ▾
- Literature search ▾
- Study selection ▾
  - Define criteria list
  - Consistency check ▾
    - Results consistency check
  - Apply criteria ▾
  - Select studies from papers
- Data extraction ▾
- Critical appraisal
- Data synthesis
- Presenting data/results


**Result of consistency check** ✕

- At this stage, the review coordinator has to decide about the adequacy of the developed criteria
- The decisions of each review team member can be retrieved by using "Results consistency check"
- If you are the coordinator of this review please press "revise criteria list" if the inter reviewer agreement is poor (be aware that the consistency check has to be redone).
- In case inter reviewer agreement is good, please proceed by using "confirm criteria list". Be aware that no changes can be made to the selection criteria anymore! Once the criteria where accepted, they can be applied to the identified reports by using "Apply criteria"
- The calculation of the kappa value based on the measuring agreement of cochrane  
For more information please click here: <http://handbook.cochrane.org/> and see Part 2, chapter 7.2.6

**Outcome**

- Kappa value: 0.945295404814
- The strength of agreement is considered to be: 'excellent'!
- Irrespective of the strength of agreement, you can revise the criteria list or proceed with the study selection

▶ Apply criteria

Consistency check evaluation (Download as Excel sheet )

▼ show results of consistency check

- Automated calculation and reporting of consistency check results

- Home
- Settings ✓
- Protocol ▾
- Literature search ▾
- Study selection ▾
  - Define criteria list
  - Consistency check
  - Apply criteria ▾
    - Title and abstract
    - Fulltext
  - Select studies from papers
- Data extraction ▾
- Critical appraisal
- Data synthesis
- Presenting data/results

**Apply criteria** ✕

- Please, determine the mode the criteria should be applied to identified reports (title/abstract and then full text OR first title, then abstract and then full text).
- Furthermore, please decide on the amount of studies that need to be allocated to the respective team members by using the toggle bars displayed below.
- In case the selection process should be performed by multiple reviewers independently from each other, move for every review team member the slider to the very right end.
- For each review team member a maximum of three ranges can be added

**Please select one apply type:**

Apply criteria to title AND abstract  
 Apply criteria FIRST to title and SECOND to abstract

**Please specify the number of references for each team member (max value 12228):**

Christian Kohl:  exclude team member

1 - 12228 (12228)
+ add range

---

Petya Stoykova:  exclude team member

1 - 12228 (12228)
+ add range

» Apply criteria to title and abstract

- The number of studies to be assessed by each reviewer can be customized
- Currently: Same reviewers will be involved at title, abstract and full-text stage
  - Possibility for an allocation of different reviewers at the different stage will be implemented in version 2.0

- Protocol
- Literature search
- Study selection**
  - Define criteria list
  - Consistency check
  - Apply criteria**
  - Title and abstract**
  - Fulltext
  - Select studies from papers
- Data extraction
- Critical appraisal
- Data synthesis
- Presenting data/results

Please insert the abstract text, if not available

**Well done!**  
You successfully rated all criteria to all references

Criteria	Yes	Unclear	No
Growing of Bt maize under open field conditions (not in laboratory or glasshouse) <small>(Study design)</small>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
Effects of Bt maize on some aspects of life history, abundance, or behaviour of non-target animals, their ecological functions (e.g. parasitization, predation, pollination, decomposition), or their species richness relative to a non-Bt control are measured. <small>(Outcome)</small>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
Non-target animals inhabiting fields (including field margins) are studied, excluding studies exclusively on the target pests <small>(Population)</small>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
Study on maize genetically modified to express one or more proteins from Bacillus thuringiensis (Cry or Vip proteins). <small>(Intervention/Exposure)</small>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
Presence of a non-Bt maize control treatment to which Bt maize is compared. <small>(Comparator)</small>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>

**Reference: # 6**

**Title** No effect of Bacillus thuringiensis corn and Bacillus thuringiensis on the predator Orius Anthocoridae)

**Abstract** Laboratory feeding studies were conducted to determine the effects on Orius insidiosus nymphs of feeding on 1-d-old European corn borer, Ostrinia nubilalis (Hubner), larvae that had ingested a diet containing Bt toxins. A commercial formulation of Bacillus thuringiensis subsp kurstaki (Dipel ES) was incorporated into a meridic diet used to feed European corn borer larvae; they then were offered as food to O. insidiosus nymphs. Immediately after adult eclosion, O. insidiosus sex was determined, body weight and length were measured, and developmental time was calculated. Another feeding study was conducted to determine the effect of Bt corn silk on mortality of immature O. insidiosus. Fresh silks of Bt and non-Bt corn plants were offered to O. insidiosus nymphs until they reached adulthood. Mortality counts were made daily. Finally, visual counts of O. insidiosus were made on Bt and non-Bt corn in fields at three locations in Kansas. The numbers of O. insidiosus nymphs and adults were recorded on 40 plants per location on two sampling dates. No significant differences occurred in developmental time, body weight, or body length of mature O. insidiosus or mortality of immature O. insidiosus when reared on European corn borer larvae that had fed on a diet containing Dipel ES. The nymphs feeding only on Bt or non-Bt corn silk suffered 100% mortality. No significant difference occurred in mortality of immature O. insidiosus when they were fed on Bt or non-Bt silk one day and on corn earworm eggs the next day. Numbers of O. insidiosus adults and nymphs in fields of Bt corn and non-Bt corn did not differ significantly in most cases. Our results suggest that Bt corn does not have a significant effect on the predator O. insidiosus.

Online application of selection criteria at title/abstract stage  
– Discrepancies will be highlighted

Study selection

- Define criteria list
- Consistency check
- Apply criteria
- Title and abstract
- Fulltext
- Select studies from papers

Data extraction

- Critical appraisal
- Data synthesis
- Presenting data/results

### Criteria

criteria	Yes	No
Non-target animals inhabiting fields (including field margins) are studied, excluding studies exclusively on the target pests (Population)	<input checked="" type="radio"/>	<input type="radio"/>
Study on maize genetically modified to express one or more proteins from <i>Bacillus thuringiensis</i> (Cry or Vip proteins). (Intervention/Exposure)	<input checked="" type="radio"/>	<input type="radio"/>
Presence of a non-Bt maize control treatment to which Bt maize is compared. (Comparator)	<input checked="" type="radio"/>	<input type="radio"/>
Effects of Bt maize on some aspects of life history, abundance, or behaviour of non-target animals, their ecological functions (e.g. parasitization, predation, pollination, decomposition), or their species richness relative to a non-Bt control are measured. (Outcome)	<input checked="" type="radio"/>	<input type="radio"/>
Experiment should be performed under open field conditions (not in laboratory or glasshouse) (Study design)	<input checked="" type="radio"/>	<input type="radio"/>
Is it a unique entry? (Duplicate check)	<input checked="" type="radio"/>	<input type="radio"/>

Reference: #146

Title: Does Bt maize cultivation affect the non-target insect community in the agro ecosystem?

Revista Brasileira de Entomologia 60 (2016) 82–93

REVISTA BRASILEIRA DE  
**Entomologia**  
A Journal on Insect Diversity and Evolution  
www.rbentomologia.com

Biological Control and Crop Protection

Does Bt maize cultivation affect the non-target insect community in the agro ecosystem?

Daniela Chaves Resende<sup>a</sup>, Simone Martins Mendes<sup>a,4</sup>, Rosângela C. Marucci<sup>b</sup>, Alessandra de Carvalho Silva<sup>c</sup>, Mônica Matoso Campanha<sup>a</sup>, José Magid Waquil<sup>d</sup>

<sup>a</sup> Embrapa Milho e Sorgo, Sete Lagoas, MG, Brazil  
<sup>b</sup> Universidade Federal de Lavras, Lavras, MG, Brazil  
<sup>c</sup> Embrapa Agrobiologia, Seropédica, RJ, Brazil  
<sup>d</sup> Consulting and Training in Integrated Pest Management, Sete Lagoas, MG, Brazil

ARTICLE INFO

Article history:  
Received 16 December 2014  
Accepted 20 November 2015  
Available online 19 December 2015  
Associate Editor: Mário A. Navarro Silva

Keywords:  
Biosafety  
GM maize  
Tri-trophic interactions  
Integrated pest management

ABSTRACT

The cultivation of genetically modified crops in Brazil has led to the need to assess the impacts of this technology on non-target species. Under field conditions, the potential effect on insect biodiversity was evaluated by comparing a homogeneous corn field with conventional and transgenic maize, expressing different Bt proteins in seven counties of Minas Gerais, Brazil. The richness pattern of non-target insect species, secondary pests and natural enemies were observed. The results do not support the hypothesis that Bt protein affects insect biodiversity. The richness and diversity data of insects studied were dependent on the location and other factors, such as the use of insecticides, which may be a major factor where they are used.

© 2015 Sociedade Brasileira de Entomologia. Published by Elsevier Editora Ltda. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Transgenic strategies for protecting crops against pests depend on the transfer and expression of defense genes to the crop species of interest. Among the most widely known and studied examples of induced resistance are those based on the use of the delta-endotoxin of the bacterium *Bacillus thuringiensis* Berliner, 1915, also known as Bt crops. This bacterium occurs naturally in soil and has the ability to form crystal proteins during the stationary and/or sporulation phase (Vasconcelos et al., 2011). After ingestion and solubilization of the crystals in the midgut of the insect its depends plants. The first case deals with a mixture of spores and crystals, sprayed on plants, and they must be activated in the gut of the insects, whereas in genetically modified (GM) plants, the protein is produced already activated in its toxic form. Thus, the question concerns those herbivorous insects that do not provide suitable conditions in their digestive tract to activate the proteins present in the bio-insecticides; may they still be affected by the toxin of the Bt transgenic plant, if they have specific receptors (Fontes et al., 2003)?

The commercial introduction of GM crops has led to the need to assess the possible impacts of this technology on the environ-

Window size can be customized

- Online application of selection criteria at full text stage
  - Discrepancies will be highlighted
- Bulk upload of pdfs possible (~500 files per upload)

- Home
- Settings
- Protocol
- Literature search
- Study selection**
  - Define criteria list
  - Consistency check
  - Apply criteria
  - Select studies from papers
- Data extraction
- Critical appraisal
- Data synthesis
- Presenting data/results

**Select studies**

- To add studies, please click on +
- Please be aware that when one reviewer started to extract studies from one report, no other review team member can add studies for this specific report.
- In order to allow for a study selection by a different review team member for this specific report, the coordinator has to reset the user by clicking on ↻

Download included references after fulltext screening: XLSX or RIS

Displaying 1-1 of 1 result.

page size: 300

#	Title
7	Humoral and cellular immune responses in mice after airway administration of Bacillus thuringiensis Cry1Ab and MON810 cry1Ab-transgenic maize <a href="#">hide studies</a>

Order	Data location	Study name	Actions
↑ ↓	Figure 1	Cry1Ab	✎ 🗑
↑ ↓	Table 2	C. elegance	✎ 🗑

» Proceed with data extraction

CADIMA facilitates the extraction of relevant studies from included records

- Home
- Settings ✓
- Protocol ▾
- Literature search ▾
- Study selection ▾
- Data extraction ▾**
  - Define critical appraisal criteria
  - Define data extraction columns
  - Perform data extraction
- ★ Critical appraisal
- Data synthesis
- Presenting data/results

**Perform data extraction**

- Data extraction can be performed on- or offline, or a mixture of both. CADIMA will automatically provide information regarding study/article ID, study authors, publication year, title and data location
- [Online data extraction](#)  
For online data extraction, please, enter the requested data in the table below. Please be aware that the each review team member can overwrite already entered data without any notification
- [Offline data extraction](#)  
For offline data extraction, please, press "download excel sheet". All data that were already entered e.g. via using the online data extraction mode, will be automatically displayed as well. Fill in the requested data and upload it again to CADIMA by using "upload excel sheet". When inconsistencies between the uploaded information and the information already entered into CADIMA occur, a notification will pop up.

Displaying 1-3 of 3 results.

page size:

Comment	Article ID	Study ID	Author	Publication Year	Title	Study Name
	1	1	Al-Deeb, M. A.; Wilde, G. E.; Higgins, R. A.	2001	No effect of Bacillus thuringiensis corn and Bacillus thuringiensis on the predator Orius insidiosus (Hemiptera : Anthocoridae)	Orius insidiosus nymphs
	1	2	Al-Deeb, M. A.; Wilde, G. E.; Higgins, R. A.	2001	No effect of Bacillus thuringiensis corn and Bacillus thuringiensis on the predator Orius insidiosus (Hemiptera : Anthocoridae)	Orius insidiosus adults
	1	3	Al-Deeb, M. A.; Wilde, G. E.; Higgins, R. A.	2001	No effect of Bacillus thuringiensis corn and Bacillus thuringiensis on the predator Orius insidiosus (Hemiptera : Anthocoridae)	Survival rate Orius insidiosus

- On- and offline data extraction possible

Article ID: 14      Study ID: 1

Fulltext: no PDF available

Author:

Title:  
Review Manager (RevMan) Version 5.3  
2014

Data Location:      Study Name:  
Figure 1      C. elegans

Comments:

Data completed

sample\_size      mean      organism

comparator

Will be displayed during critical appraisal



- Home
- Settings ✓
- Protocol ▾
- Literature search ▾
- Study selection ▾
- Data extraction ▾
- Critical appraisal ▾
- Settings
- Results critical appraisal
- Data synthesis
- Presenting data/results

**Apply critical appraisal criteria to study**

- Rate each criteria to the study
- Use "next" or "back" buttons at the bottom to go on

**Study information**  
 Title: No effect of Bacillus thuringiensis corn and Bacillus thuringiensis on the predator Orius insidiosus (Hemiptera : Anthocoridae) (2001 ) Authors: Al-Deeb, M. A.; Wilde, G. E.; Higgins, R. A.  
 Article ID: 1 Study ID: 1  
 Data location: Table 3 Study name: Orius insidiosus nymphs

✖ Abort and back to list
◀ Previous
Next ▶
💾 Save and back to list

**Critical appraisal criteria**

criteria	Risk
Cultivars used: Low risk if corresponding near-isolines are used for Bt and conventional treatments, high risk if distantly related cultivars are used <small>(1 - 3)</small>	<input style="width: 80%;" type="text" value="2 [ Low ]"/> <small>show / make comment ▾</small>
Sampling methods: High risk if different methods are used to measure animal populations in the different treatments, low risk if the same method was used <small>(1 - 3)</small>	<input style="width: 80%;" type="text" value="2 [ Low ]"/> <small>show / make comment ▾</small>

**Data extraction information (Download file)**

Critical appraisal column	Value of data extraction
Control_cultivar_used	near isogenic variety
Sampling_method_control	manual counting
Sampling_method_experimental	manual counting

CADIMA support the critical appraisal of included studies

# CADIMA assures for a thorough documentation



Home
Settings ✓
Protocol ▾
Literature search ▾
Study selection ▾
Data extraction ▾
Critical appraisal
Data synthesis
<b>Presenting data/results</b>

## Presenting data and results

- CADIMA assures for a thorough documentation of the entire review process.
- Under "Flow diagram" the study selection is depicted
- Under "Data files", CADIMA does provide all information allowing for a detailed documentation of the review process. Furthermore, review team members can decide on the information that can/should be made publically available by uploading them to "Data and results" and ticking the "public" box

Flow diagram Data files

## Files generated by CADIMA

Description	Download (file type)
Flow diagram	Flow diagram (docx)
Table displaying the results of the literature search per search string and database	Results literature search (docx)
Reference lists: database a, database b etc. and the final merged reference list or Final reference list for reference management tools	Reference list (xlsx) or Reference list for reference management tools (RIS)
List of selection criteria	Selection criteria (docx)
Consistency check evaluation Outcomes study selection at the different stages Included references after title/abstract screening Included references after full text screening	Consistency check evaluation (xlsx) Study selection outcome (xlsx) Included references title/abstract (xlsx) Included references full text XLSX or RIS
List of critical appraisal criteria	Critical appraisal criteria (docx)
Compiled data extraction sheet	Data extraction sheet (xlsx)
Outcomes critical appraisal	Critical appraisal outcome (xlsx)

# Outlook



- Version 2.0 March 2018
  - Automated duplicate removal
  - Flexibility during screening stage
- Support rapid evidence syntheses
  - Adapt the approach to the synthesis purpose
  - Want to contribute: contact [christian.kohl@julius-kuehn.de](mailto:christian.kohl@julius-kuehn.de)
- User feedback
  - Test CADIMA
  - Register to online workshops

# Acknowledgement



Ralf Wilhelm  
Joachim Schiemann

**Consulting**  Collaboration for  
Environmental  
Evidence

Andrew Pullin  
Neal Haddaway

## Technical support:

**JKI, DV – Q**  
Stefan Unger  
Steffen Kecke  
Christian Müller  
Simone Frenzel