Erasmus MC
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A European perspective to networking in drug safety, EU-ADR as example

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The EU-ADR Project

(formerly known as ALERT)

Exploring and **U**nderstanding **A**dverse **D**rug **R**eactions by Integrative Mining of Clinical Records and Biomedical Knowledge

http://euadr-project.org/

Started February 2008

EC- Grant agreement no.: 215847

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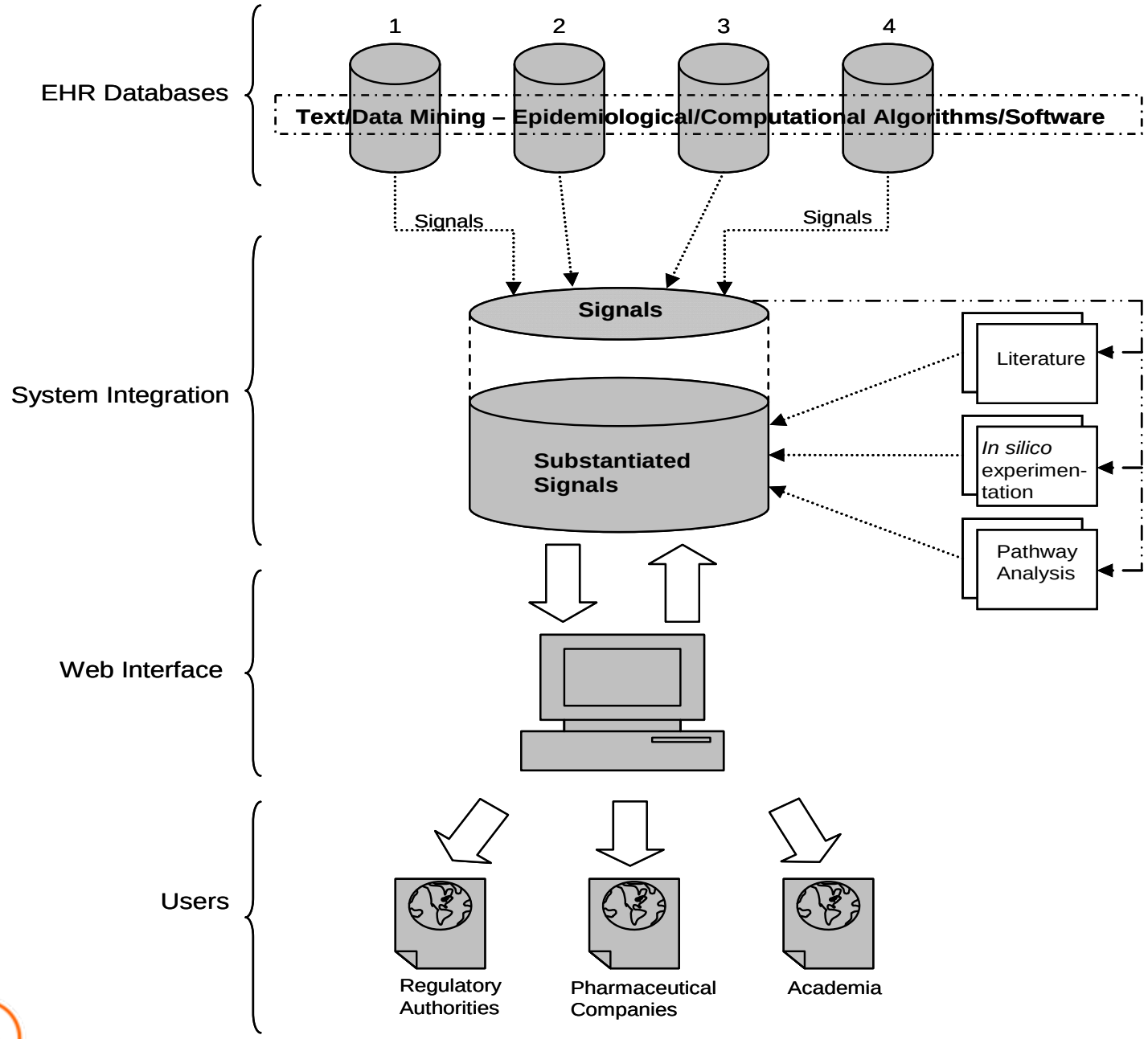
SEVENTH FRAMEWORK PROGRAMME

eu-adr

The overall objective of EU-ADR is:

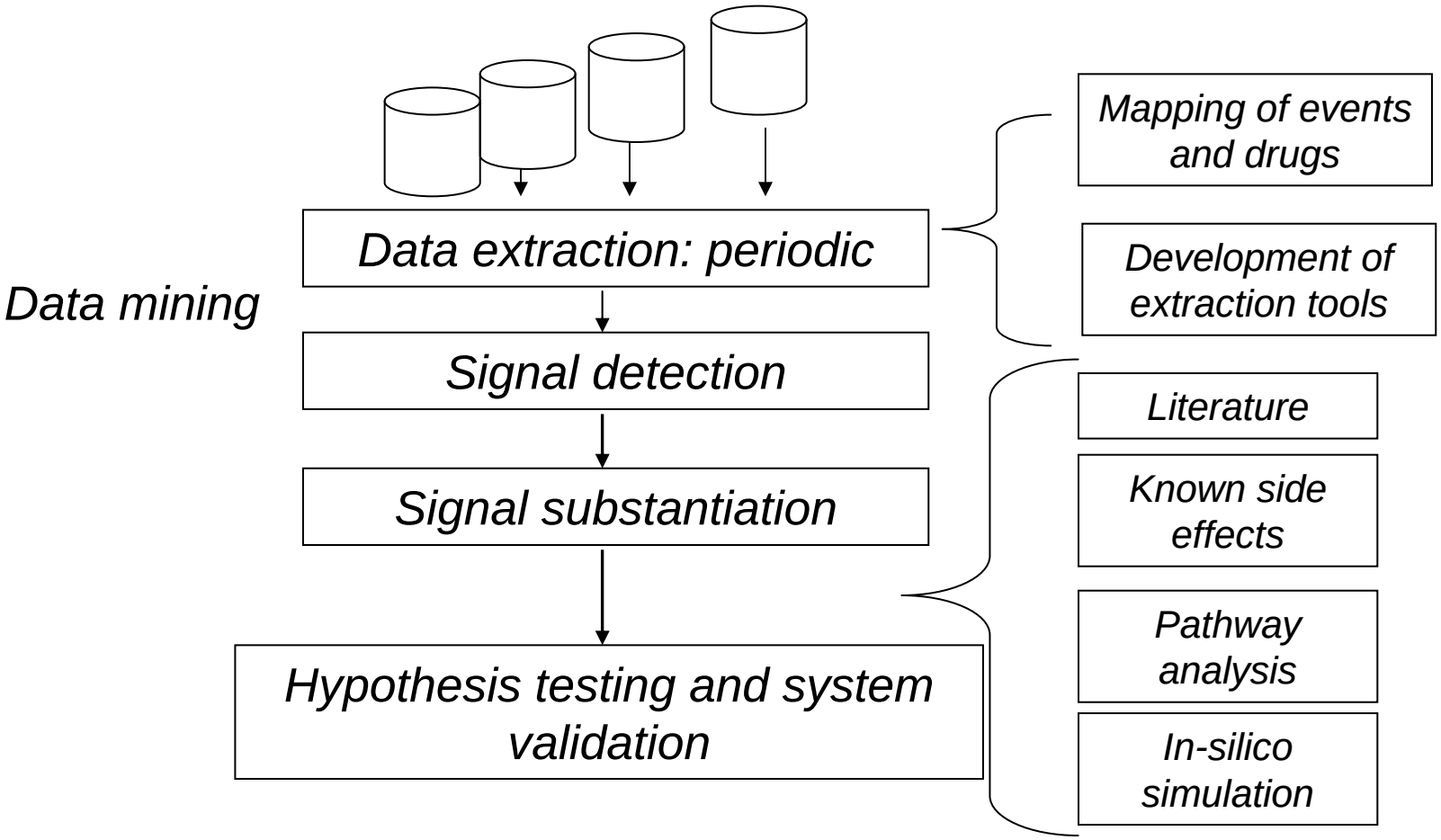
The design, development and validation of a computerized system that exploits data from *electronic healthcare records* and *biomedical databases* for the *early detection of adverse drug reactions*.

Supposed to be complementary to existing systems, have more power and detect signals earlier


EHR Databases
1
2
3
4
Text/Data Mining – Epidemiological/Computational Algorithms/Software
Signals
Signals
System Integration
Signals
Substantiated Signals
Literature
In silico experimen-tation
Pathway Analysis
Web Interface
Users
Regulatory Authorities
Pharmaceutical Companies
Academia

EU-ADR concept

8 Medical record and claims databases:
Now 30 Million persons (IT, NL, UK, DK)



www.euadr-project.org

Key objectives and achievements

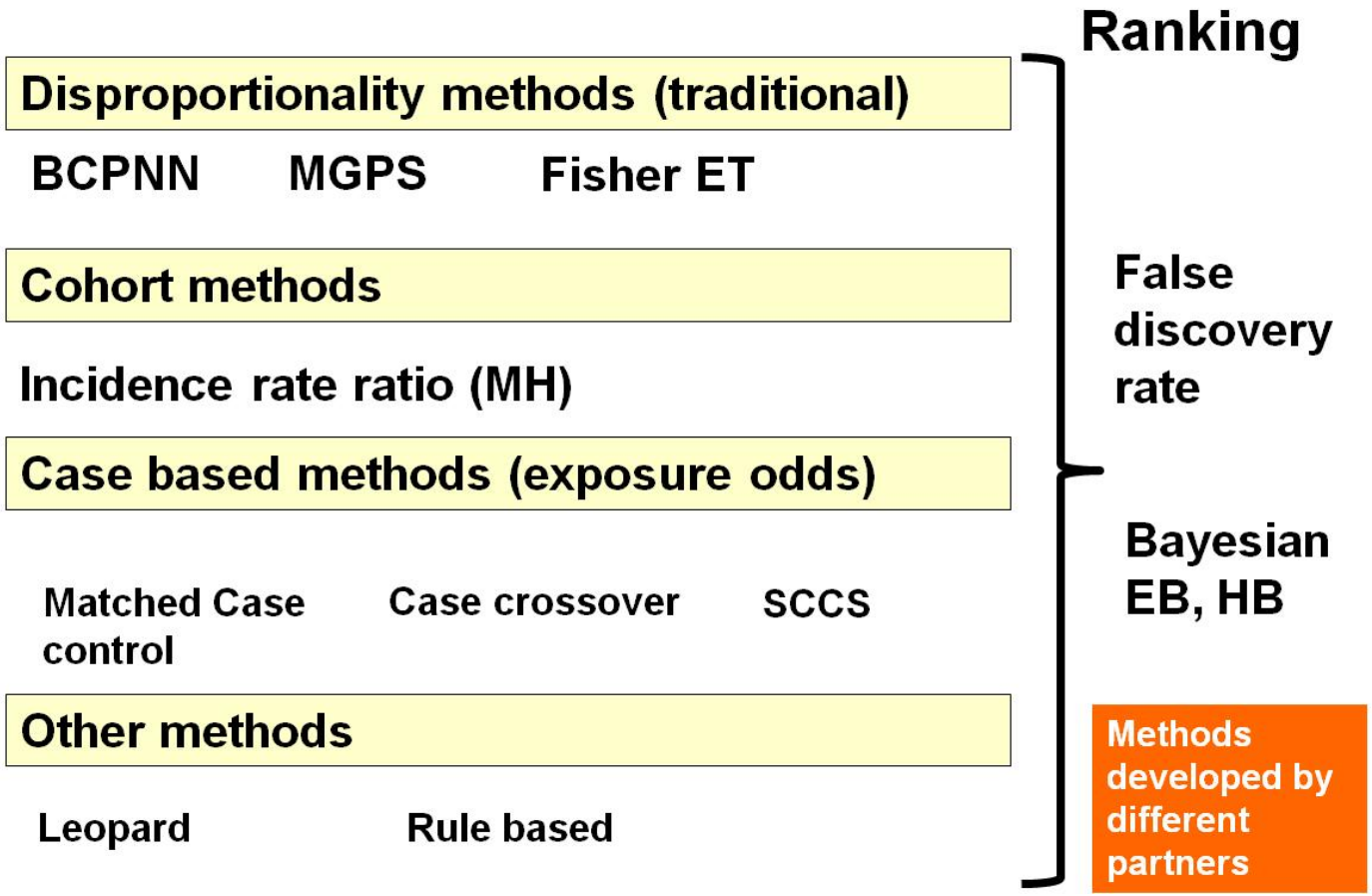
- To define a list of important adverse events that should be monitored.
  - Delivered and published 23 events (Trifiro' et al. PDS 2008)
- To compile validation sets of signals (true positive and true negative drug-event combinations), to be used throughout the project for learning and testing purposes.
  - Delivered (60 pairs, currently being extended)
- To provide a mapping between the different terminologies used in the EHR systems
  - Delivered and published: all based on UMLS (Avillach P et al. JAMIA)
  - Benchmarking ongoing and has been tested also with US/Asian data, presented at ICPE 2009
  - Harmonization and benchmarking done for 6 events/ ongoing for other 6

Key objectives and achievements

- **To establish a common data framework that allows for extraction of the relevant data from each EHR system for subsequent text and data mining processing.**
  - Distributed data network approach chosen
  - Jerboa software (JAVA based) developed which locally elaborates common input files to generate de-identified data (flexible script)
  - 100 million person-years currently combined (8 databases)
  - Jerboa program used in multiple other EC-funded projects, across US and ASIA and in the H1N1 safety studies
  - Data mining done for all drugs against 6 (harmonized) events
- **To develop text mining techniques that detect the selected medical events in free-text and map these terms to corresponding standard codes.**
  - Work ongoing to be delivered in the coming year

Key objectives and achievements

- To develop data mining algorithms that produce a prioritized set of adverse drug reaction signals.
  - Work in progress: EU-ADR has won the OMOP cup for signal detection methods
  - Comparison of methods is being conducted to be delivered next year



Key objectives and achievements

To automatically detect scientifically and mechanistically sound explanations for the drug-event pairs by means of a combination of analyses of repositories of known side effects, biomedical literature, in silico predictions and pathway mapping.

Repositories of known side effects: webservice working
Biomedical literature: protein mapping: done and working webservice
In silico predictions of targets: running webservice
Pathway mapping: fine-tuning is ongoing
Next year we will deliver information on the validity

To develop a computerised system that integrates the different software components and adds a web interface for seamless access to the knowledge created by the project.

System designed and security being dealt with, will be delivered in coming year; currently being tested for different use scenarios

Key objectives and achievements

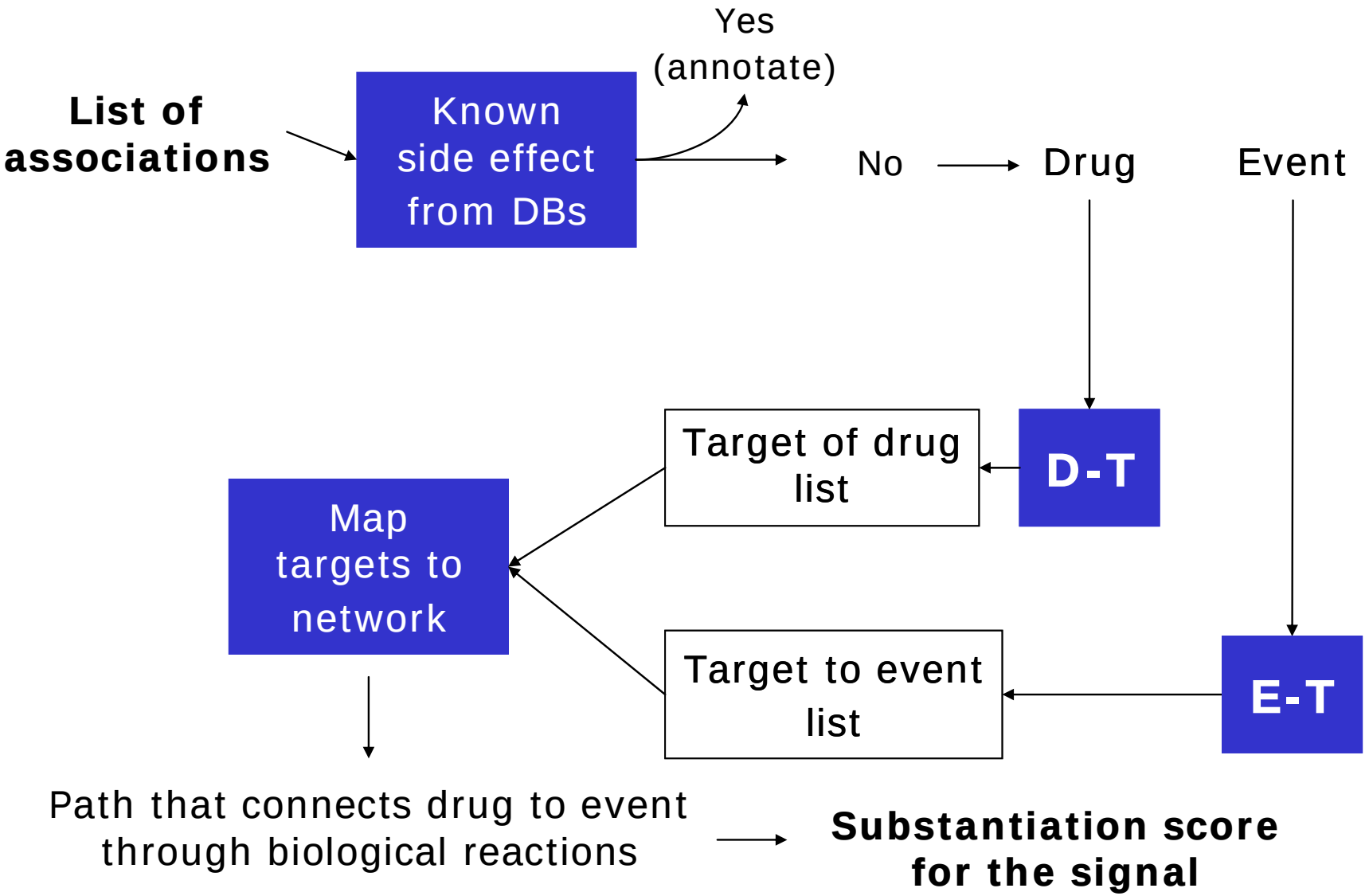
To perform retrospective and prospective validation of the system and the results.

Event validation: to be done in coming year, chart review for positive predictive values

Comparison between signals detection in EU-ADR and in FDA-AERS/WHO
in terms of complementarity and velocity

Hypothesis testing studies
New signals will be tested according to properly designed studies using the UE-ADR platform

Signal substantiation (automated)



Implications for Sentinel

- No direct implications rather opportunities

- Signal detection methods evaluation
- Comparison of system with existing spontaneous reporting systems
- Computerized system might be used by FDA (starts with a drug-event list)
- Signal substantiation pipeline could be useful for Sentinel system

- Common data input files might be exchanged between US and EU to allow for upscaling and collaboration
- Benchmarking is useful method of improving transparency for all databases

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