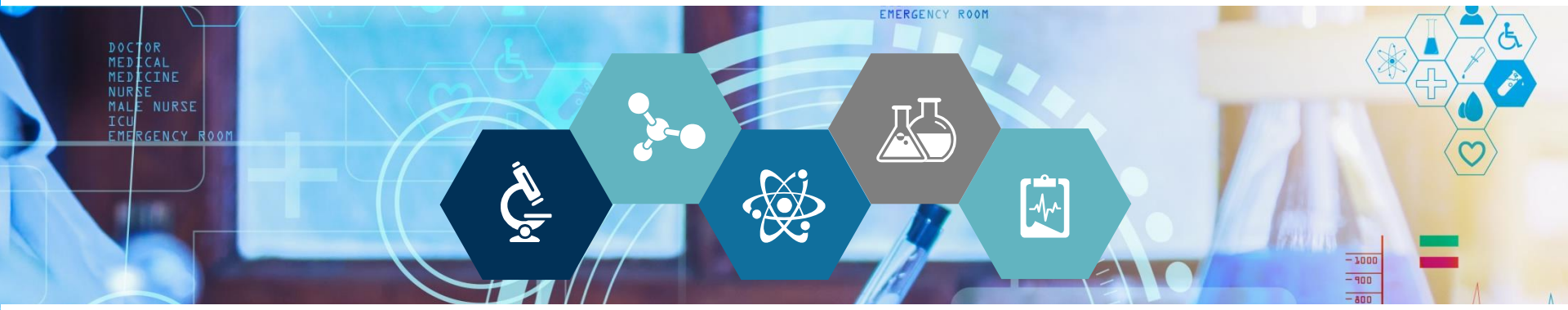
1st International Conference
Modern research trends in biomedical sciences: a holistic approach to healthcare
Institute of Health Sciences, University of Opole, Poland



Information technologies as a tool for identification of endocrine disrupting chemicals

Milen Todorov, assoc. prof., PhD
University "Prof. Dr. Assen Zlatarov", Burgas, BULGARIA

April 2024

Highlights:

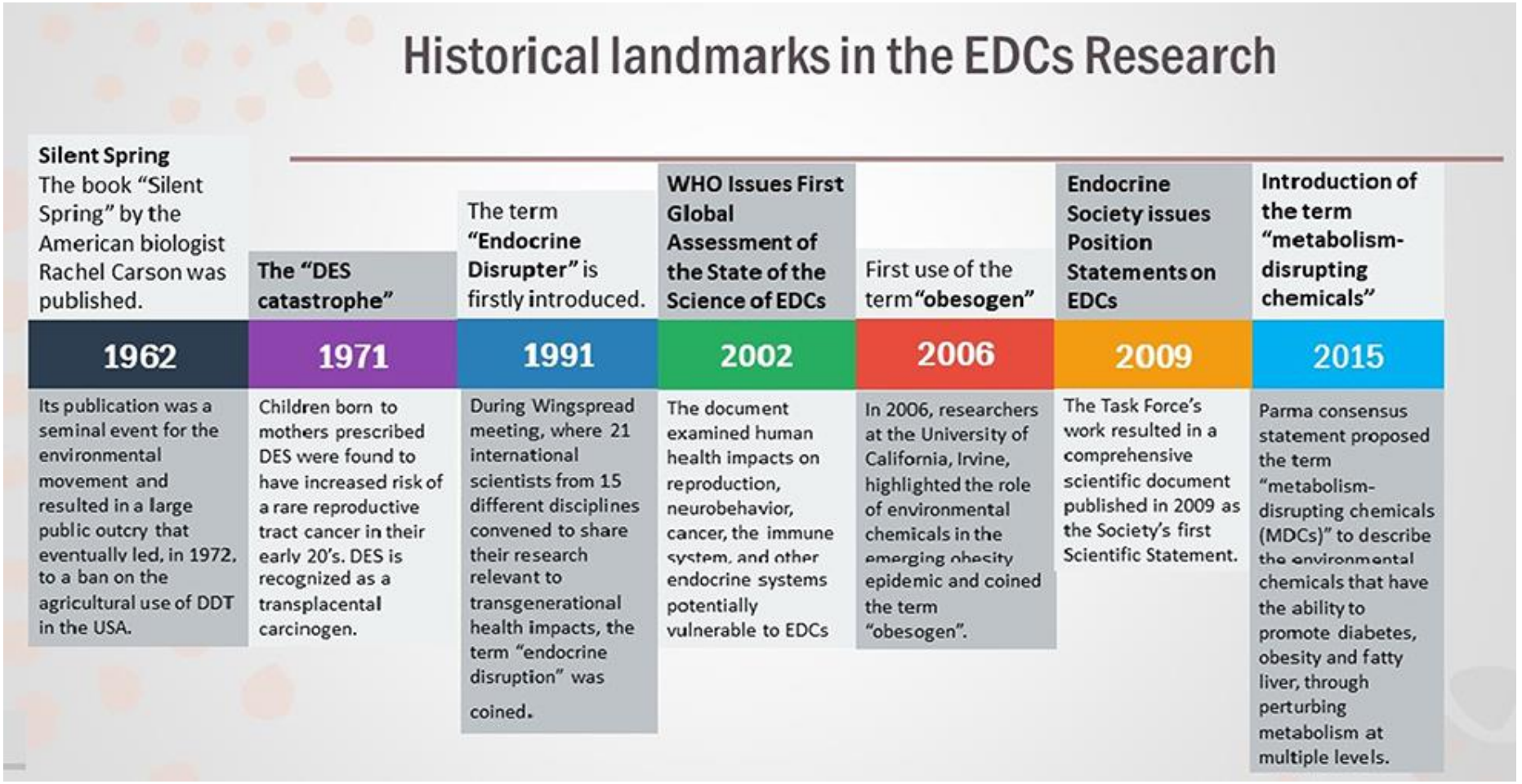
- Human health and global chemical safety
- Recent achievements in computational chemistry
- Application of computer tools for identification of estrogen disrupting chemicals (EDC)

Presentation

Summary

- **Landmarks in EDC Research and computational chemistry**
- Prediction the binding effect of chemicals toward the estrogen receptor
- Conclusions

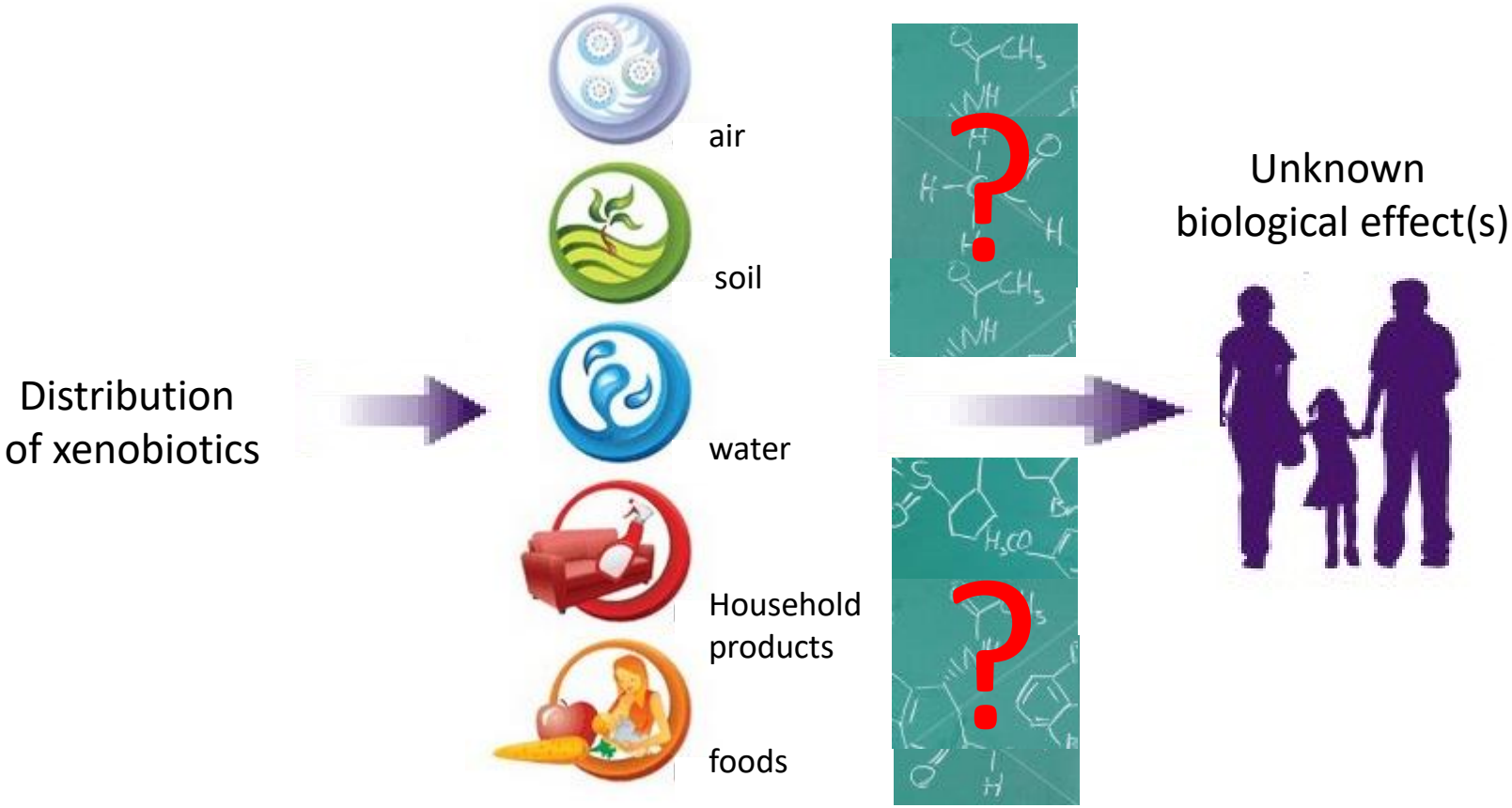
EDC Research Timeline



https://doi.org/10.3389/fendo.2019.00112

Computational chemistry and human health

Xenobiotics in the environment



Computational chemistry and human health

How many chemicals are available in the EU environment

?

Do we know their possible biological/toxic effect(s)

Computational chemistry and human health

European CHemicals Agency
Helsinki, Finland

REACH is the European Regulation on Registrtion, Evaluation, Authorisation and Restriction of Chemicals.

It entered into force in 2007, replacing the former legislative framework for chemicals in the EU.

Computational chemistry and human health

European CHemicals Agency
Helsinki, Finland

REACH is the European Regulation on Registrtion, Evaluation, Authorisation and Restriction of Chemicals.

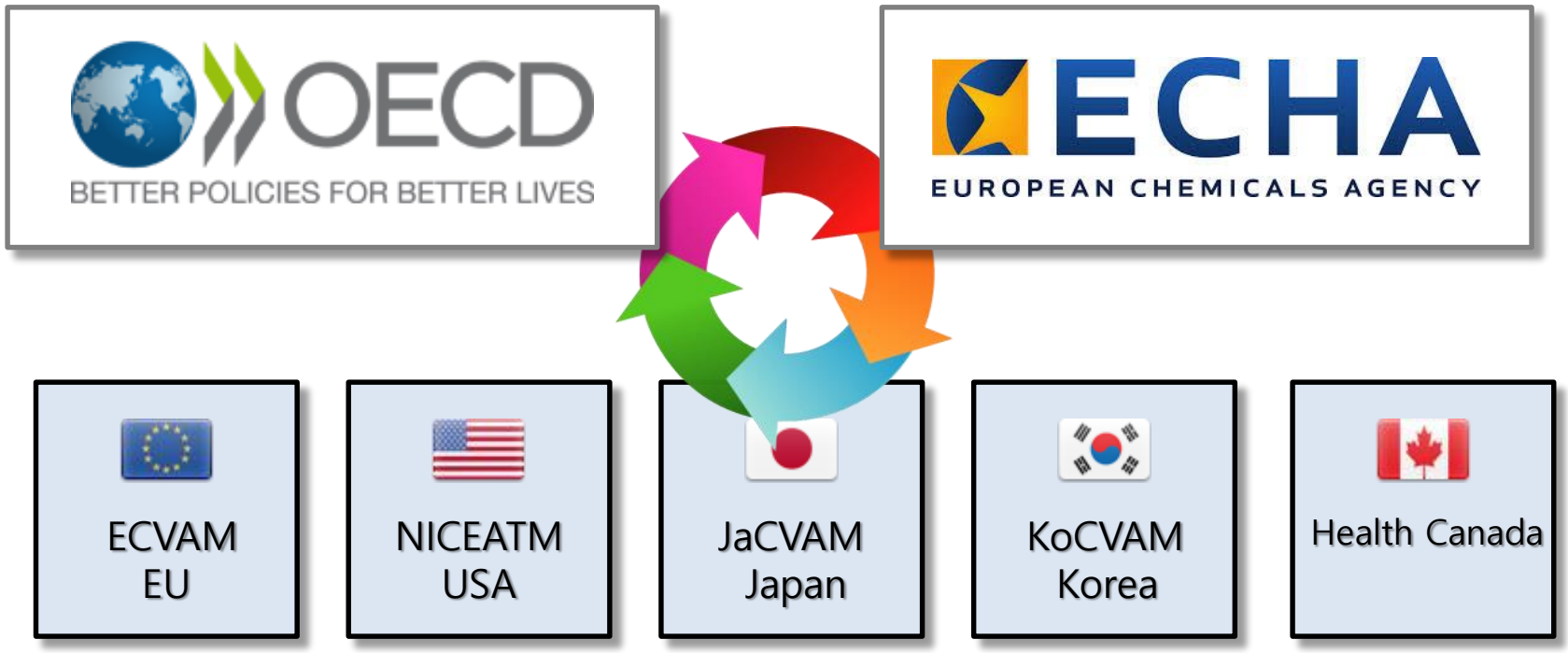
It entered into force in 2007, replacing the former legislative framework for chemicals in the EU.

The Aim is to evaluate the potential risk to human health of **30,000 chemicals** used in sufficiently high volume (1 tonne or more per year).

Computational chemistry and human health

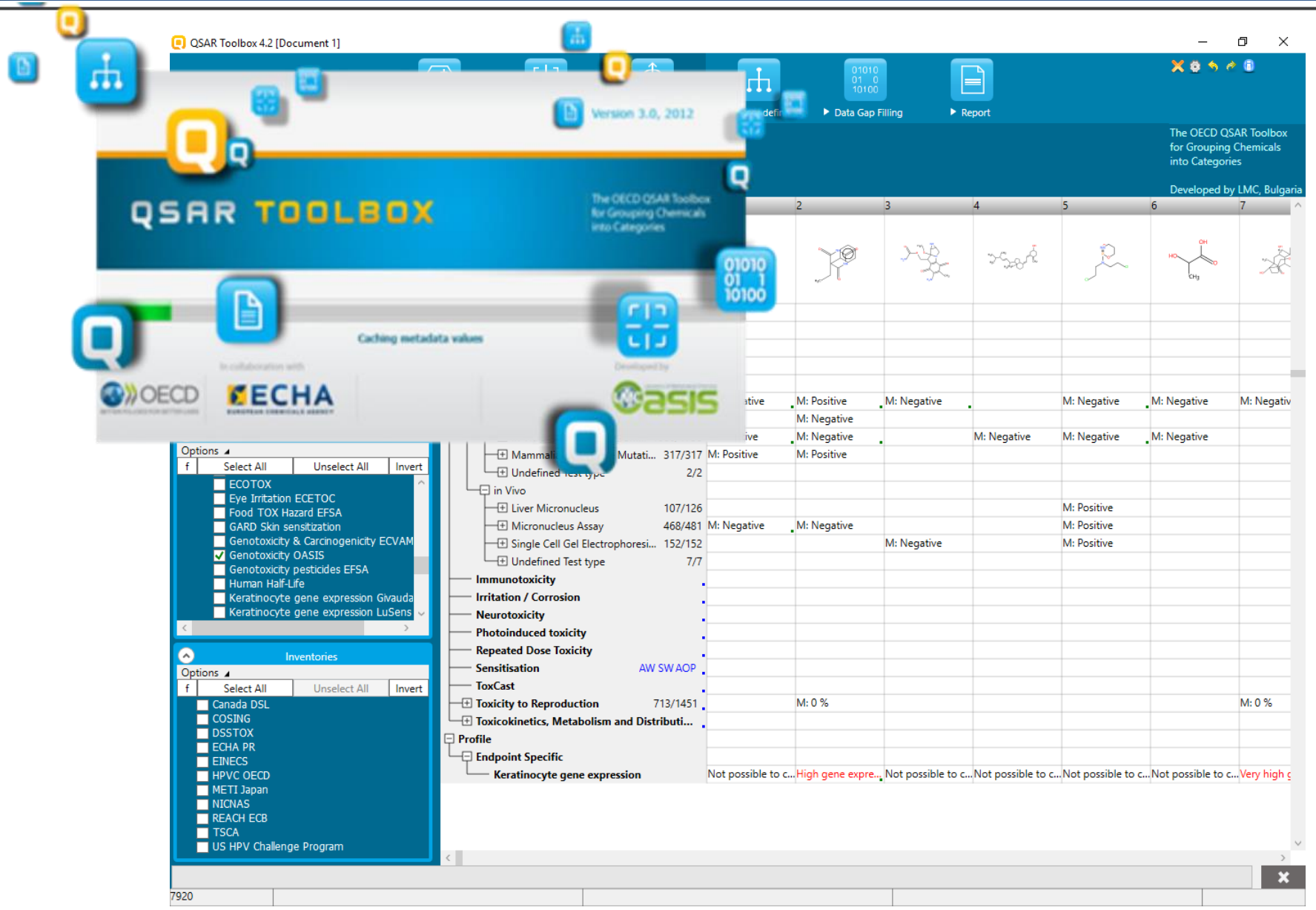
The main question is how to assess the potential risk of those **30,000 chemicals** to harm human health?

Computational chemistry and human health



The REACH legislation allows assessment of the chemicals based on alternative non-testing methods. In this respect a non-commercial software tool called OECD QSAR TOOLBOX have been developed and used for prediction of variety biological/toxic effects.

Computational chemistry and human health



Main actions performed by the Toolbox:

- Indicates if a chemical is included in national/regional regulatory inventories or existing chemical categories.
- Searches for available experimental results for the chemical of interest.
- Explores a chemical list for possible similar chemicals.
- Extracts experimental data for similar chemicals.
- Allows user to construct and apply their own models

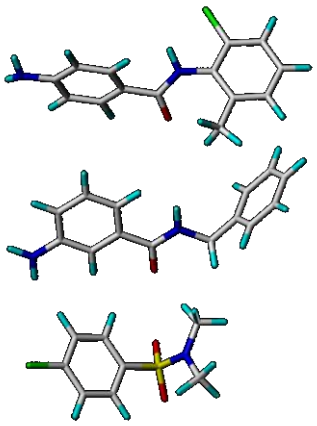
Summary

- Landmarks in EDC Research and computational chemistry
- **Prediction the binding effect of chemicals toward the estrogen receptor**
- Conclusions

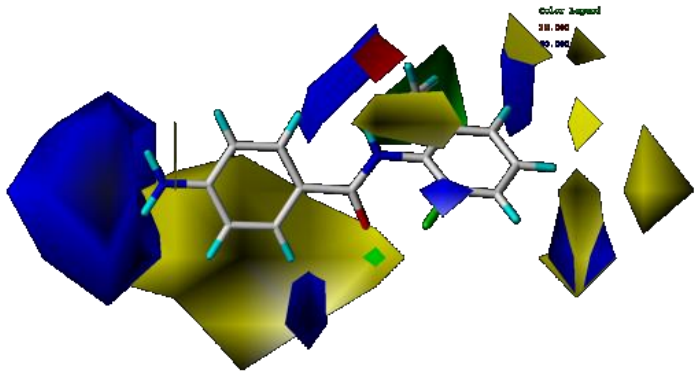
QSAR method for idenstification of EDCs

Structure — **(Q)SAR** — **Effect**

Molecule

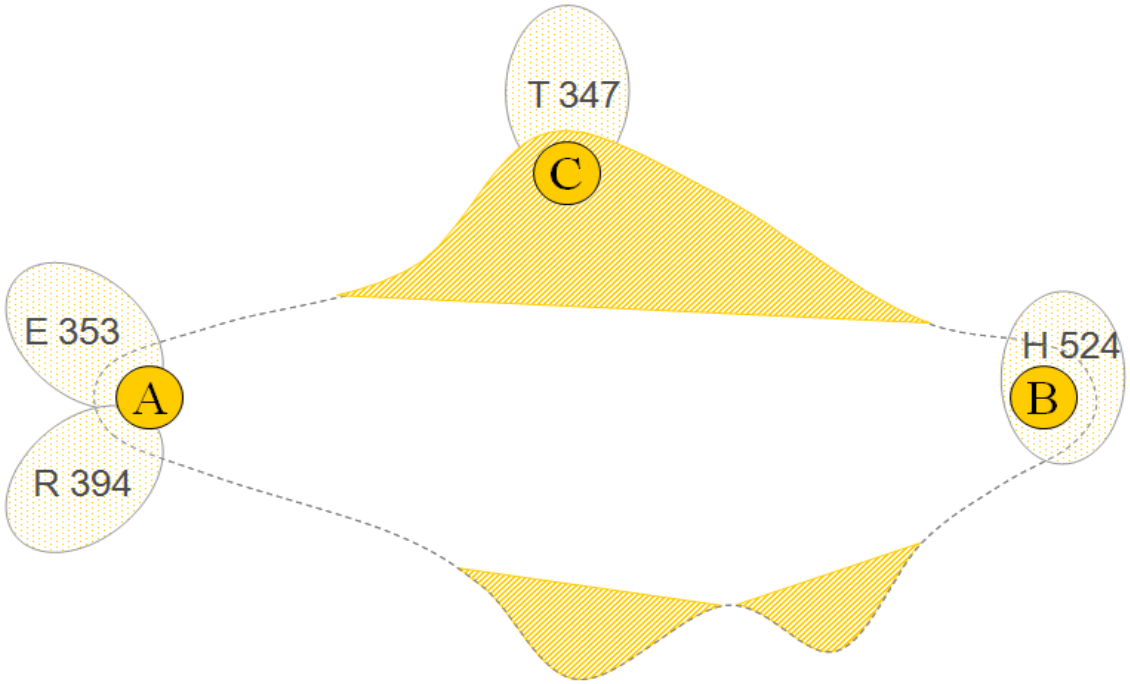


Chemical



Specificity of receptor-ligand interactions
Schematic representation of ER binding pocket

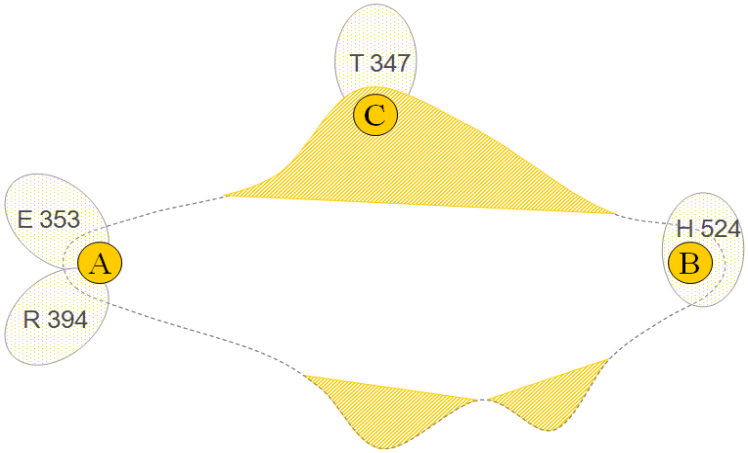
- Recognized are three sites of interaction within the pocket*

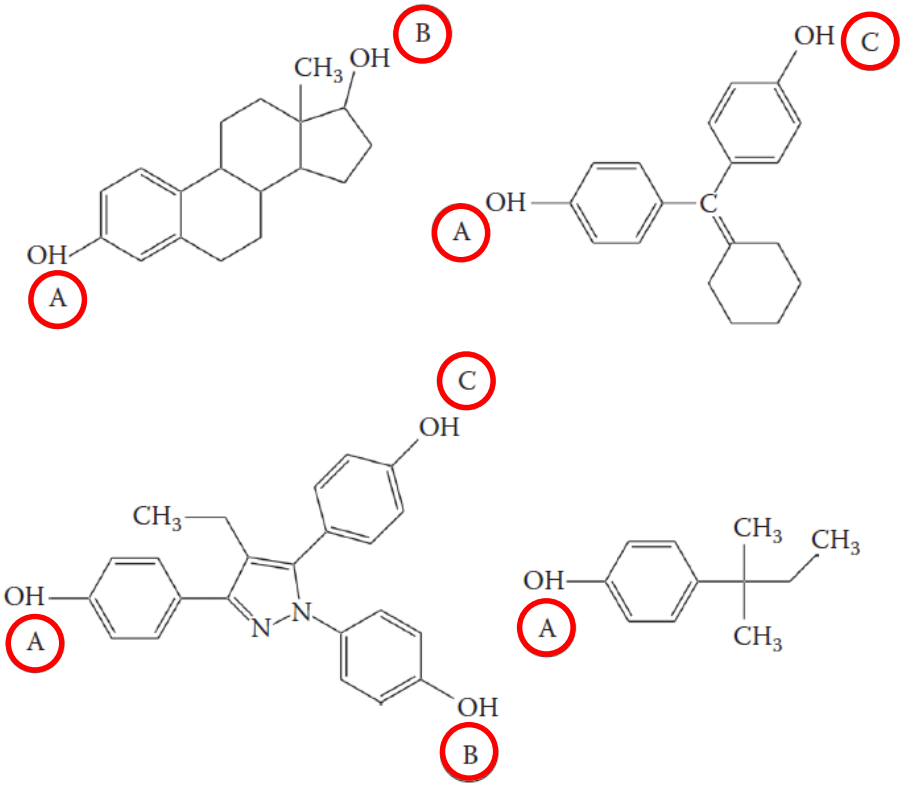


*Katzenellenbogen et al., 2002

Prediction the binding effect of chemicals toward the estrogen receptor

Specificity of receptor-ligand interactions

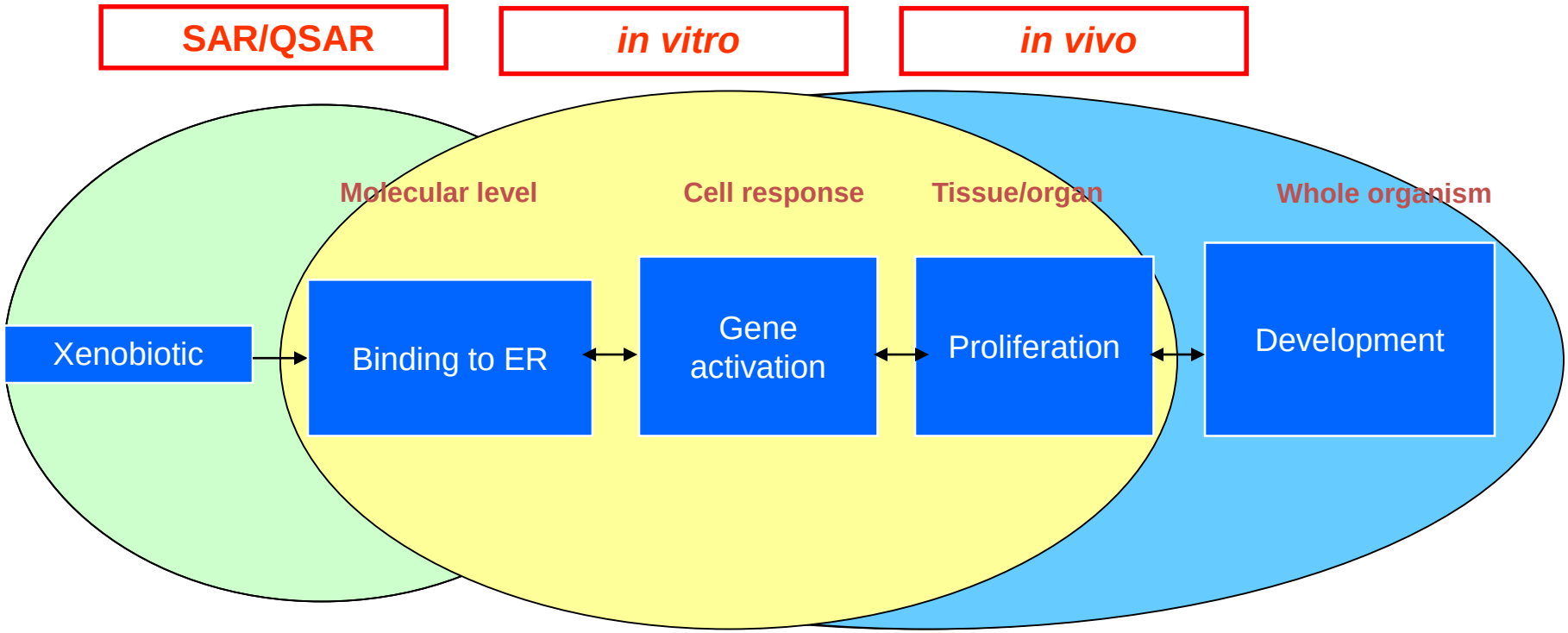




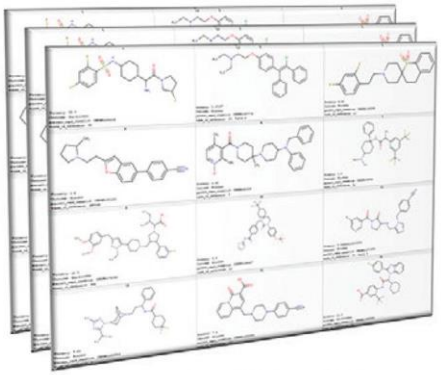
Prediction the binding effect of chemicals toward the estrogen receptor

Steps in Estrogen hormon-receptor function

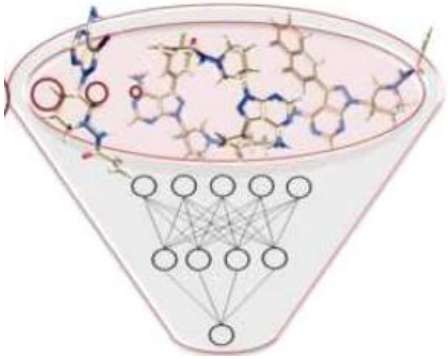
Stimulates development and maintenance of female sexual characteristics.



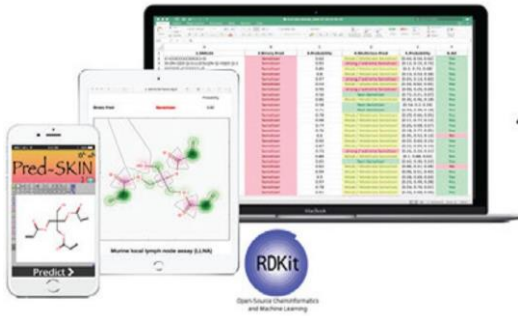
Modelling steps and prediction of EDCs



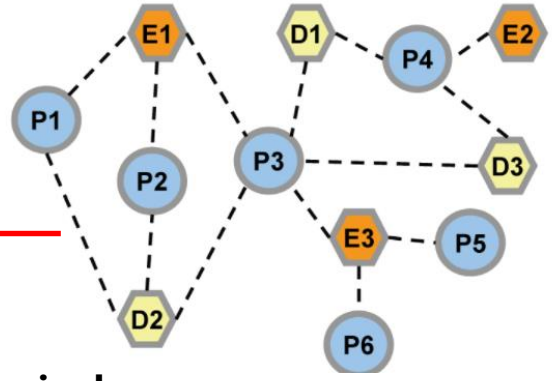
Databases
(experimental data)

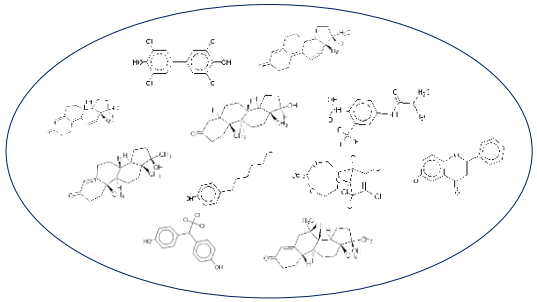


Model building

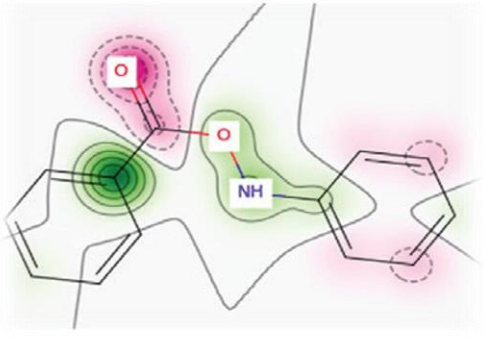


In silico model



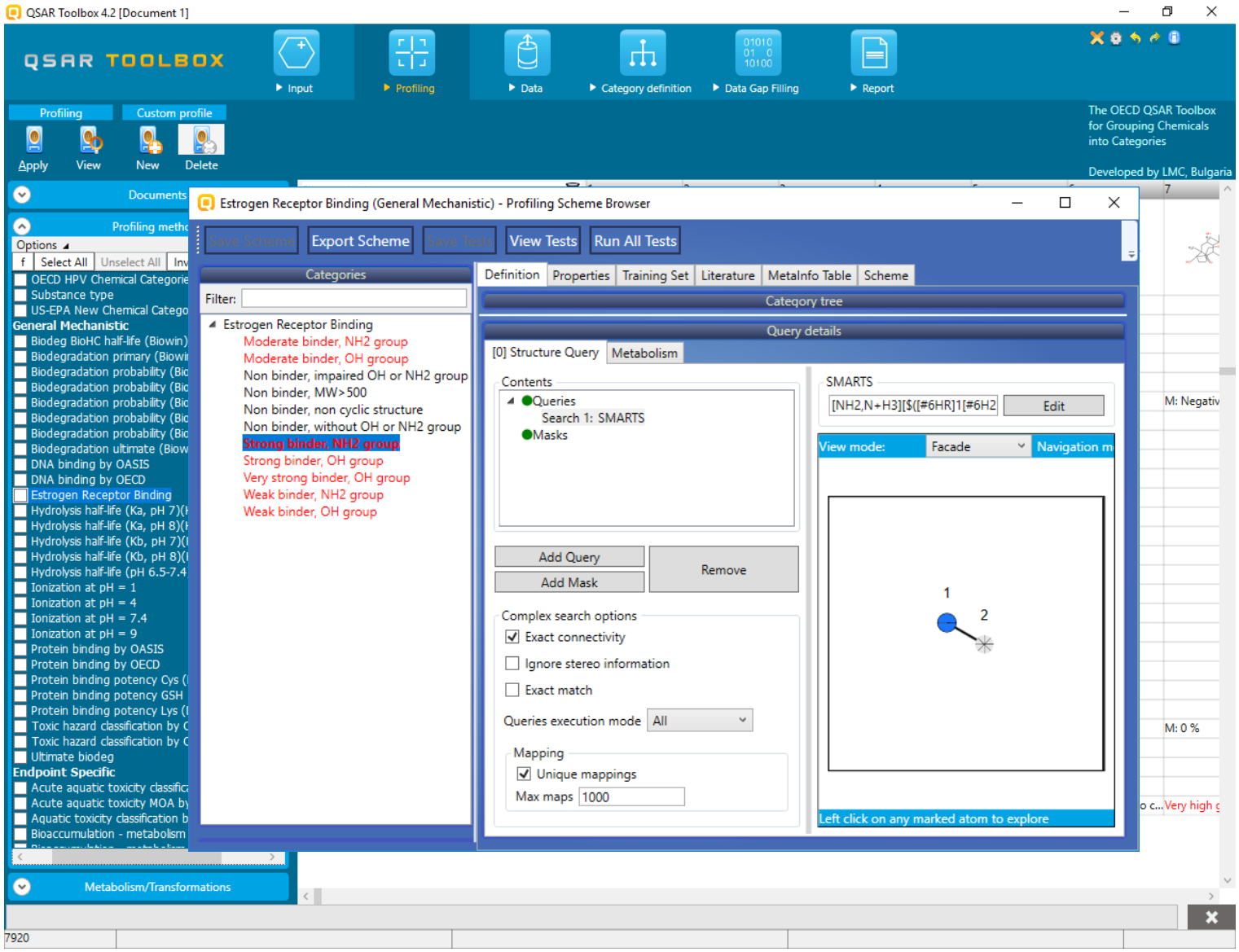


Prediction of EDC chemicals

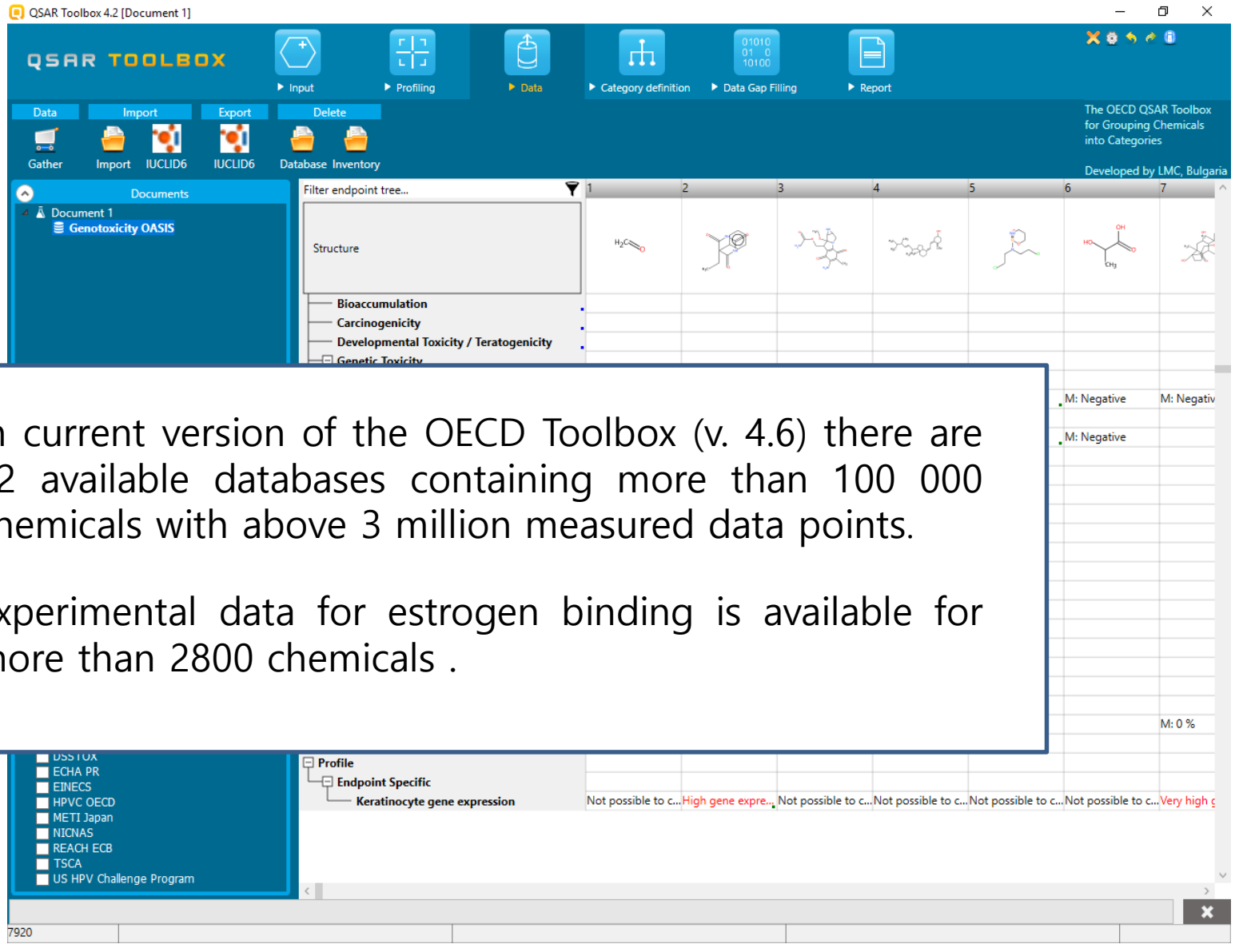


Explanation the
mechanism of effect

Prediction the binding effect of chemicals toward the estrogen receptor



Prediction the binding effect of chemicals toward the estrogen receptor



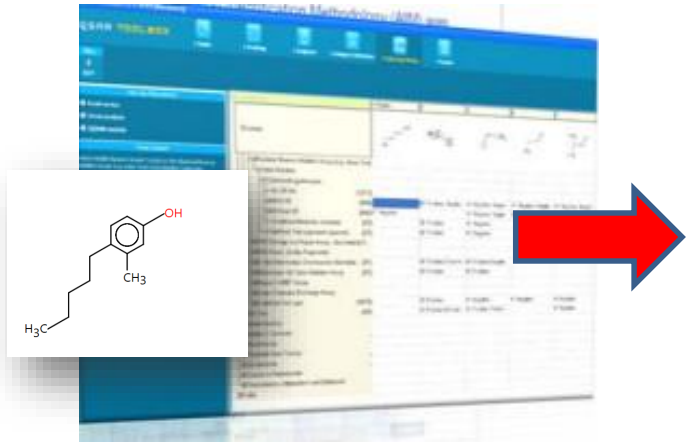
In current version of the OECD Toolbox (v. 4.6) there are 62 available databases containing more than 100 000 chemicals with above 3 million measured data points.

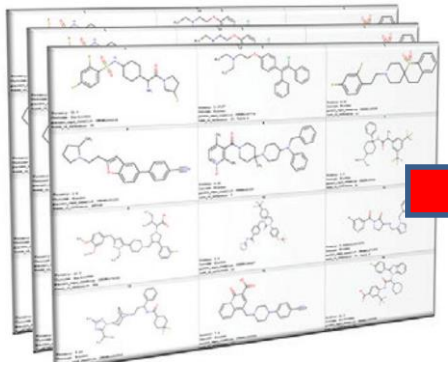
Experimental data for estrogen binding is available for more than 2800 chemicals .

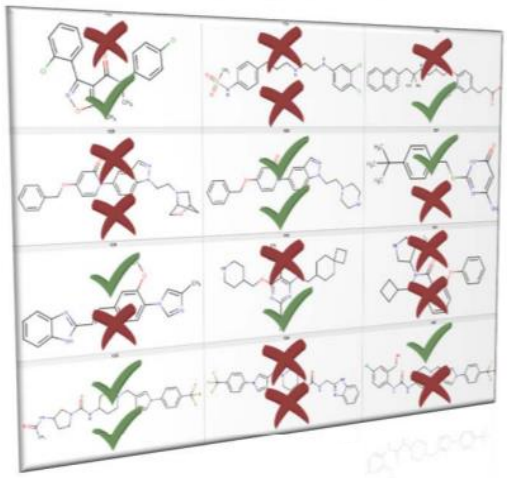
Prediction the ER binding effect of specific chemical

Case study for ***3-methyl-4-pentylphenol***

If data is not available







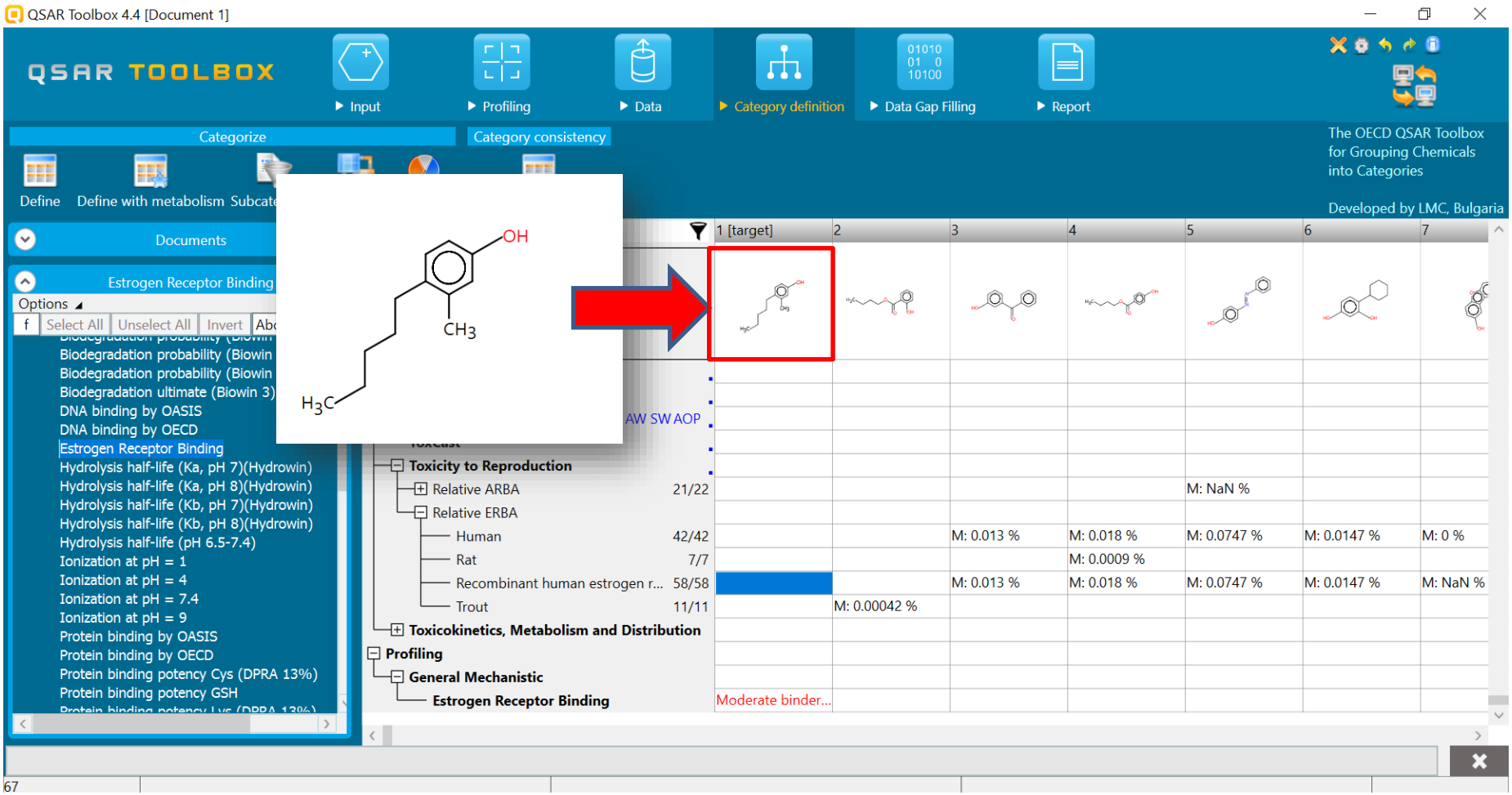
1) Input target chemical

2) Search for experimental data

3) Applying rules or model for prediction

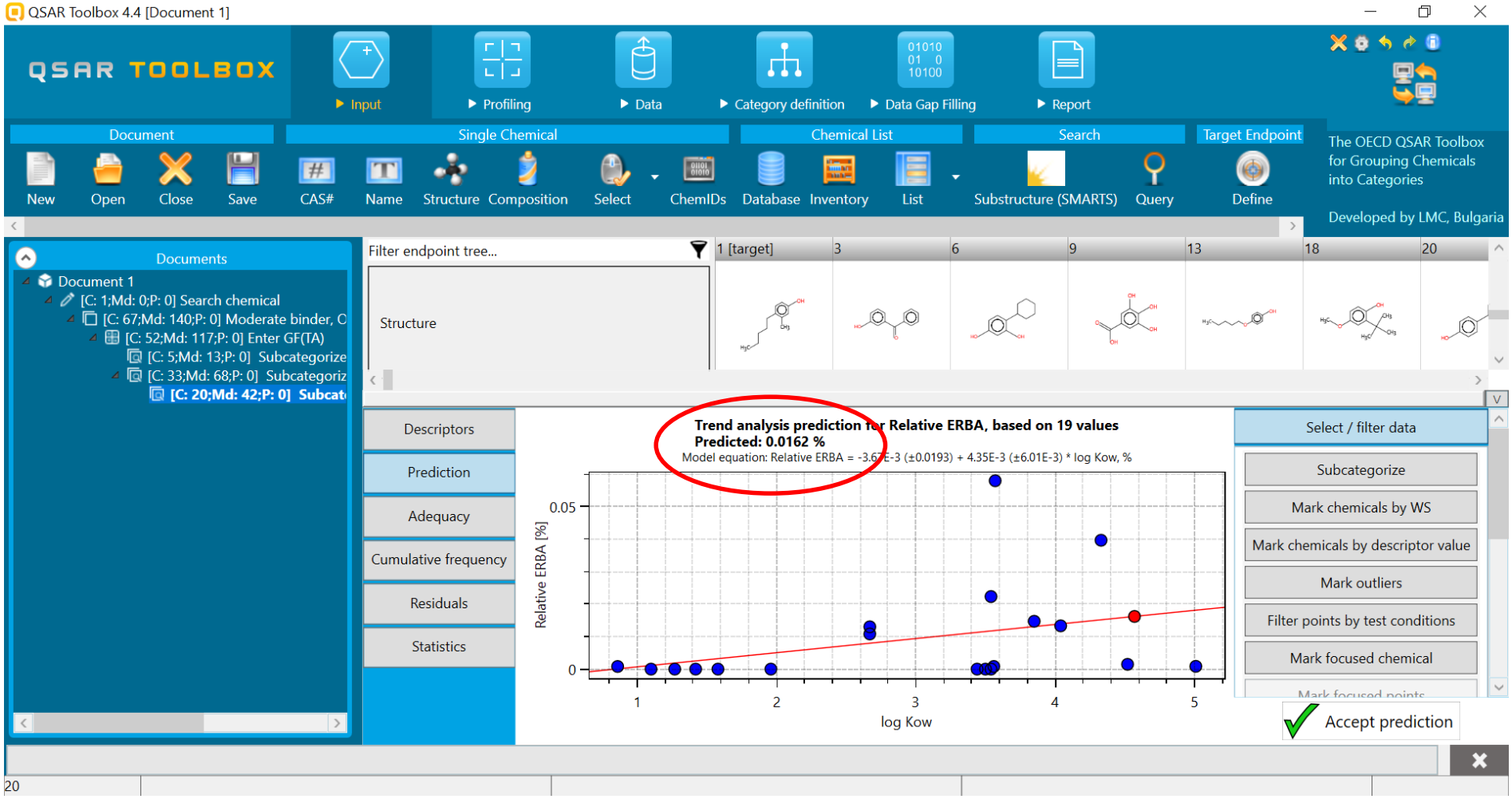
Prediction the ER binding effect of specific chemical

Case study for ***3-methyl-4-pentylphenol***



Prediction the ER binding effect of specific chemical

Predicted as weak binder to the estrogen receptor



CONCLUSIONS

- Computational tools could be used successfully for identification of EDCs
- Users of the QSAR Toolbox software are able to apply different techniques for predictions
- Theoretical predictions reduces significantly financial resources for experimental tests

Thank you for your attention!

Milen Todorov
University "Prof. Dr. Assen Zlatarov", Burgas, BULGARIA