

Safety assessment of Berberine

Corrado Lodovico Galli - ERT

Unit of Toxicology and Risk Assessment,

Department of Pharmacological and Biomolecular Sciences "Rodolfo Paoletti", Università degli Studi di Milano

President CTS Foundation For Botanical Research (FBR)

Thursday 16, 2026 - Milan

METHOD

Risk Analysis

WHO/UNEP/ILO, ICPS 1980 - FAO/WHO 1985 - EUD 93/67/EEC of 20.07.1993

RISK ANALYSIS PARADIGM



HAZARD IDENTIFICATION

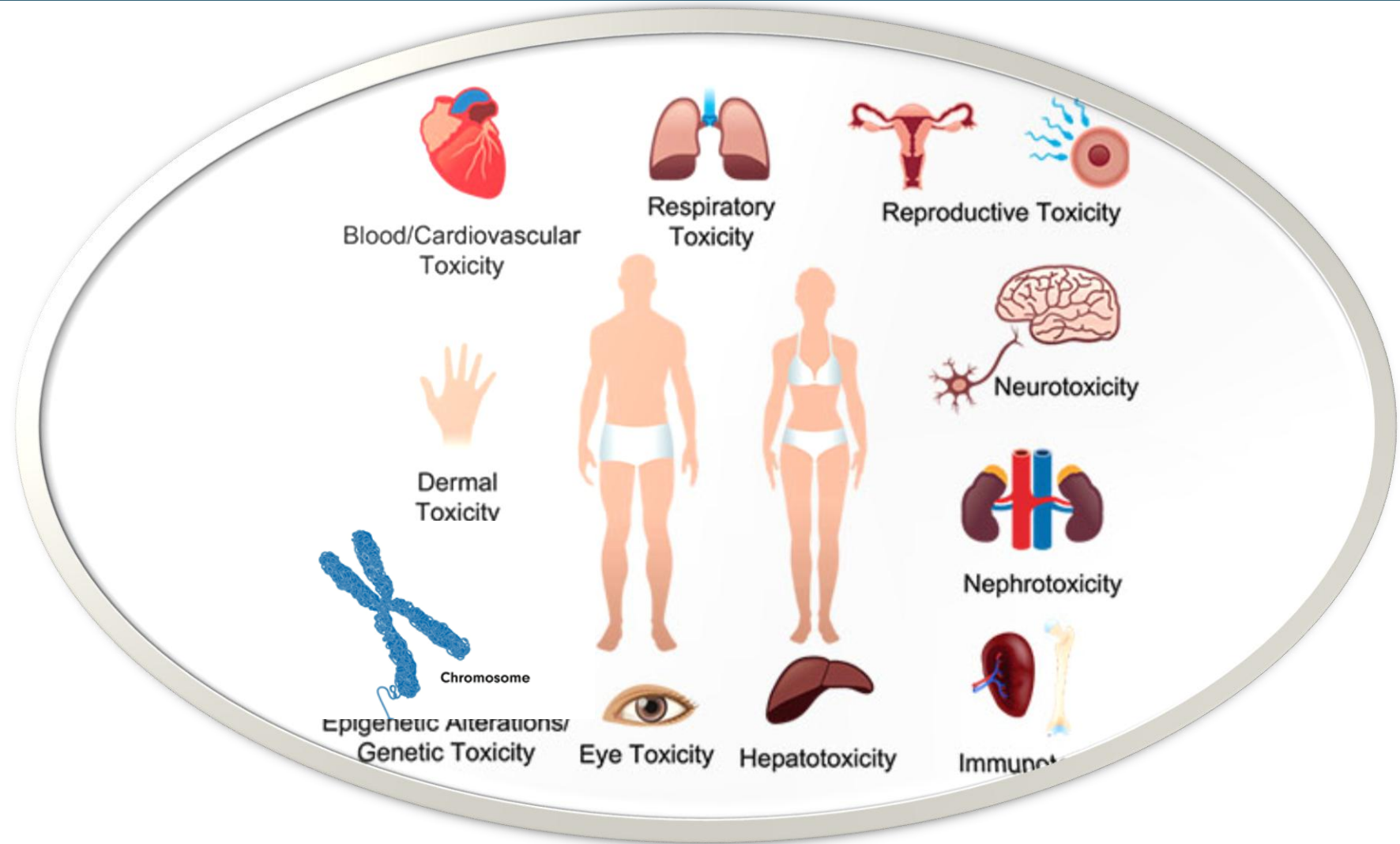
- Local toxicity

- ✓ Skin irritation
- ✓ Eye irritation
- ✓ Skin sensitization
- ✓ Photo-toxicity

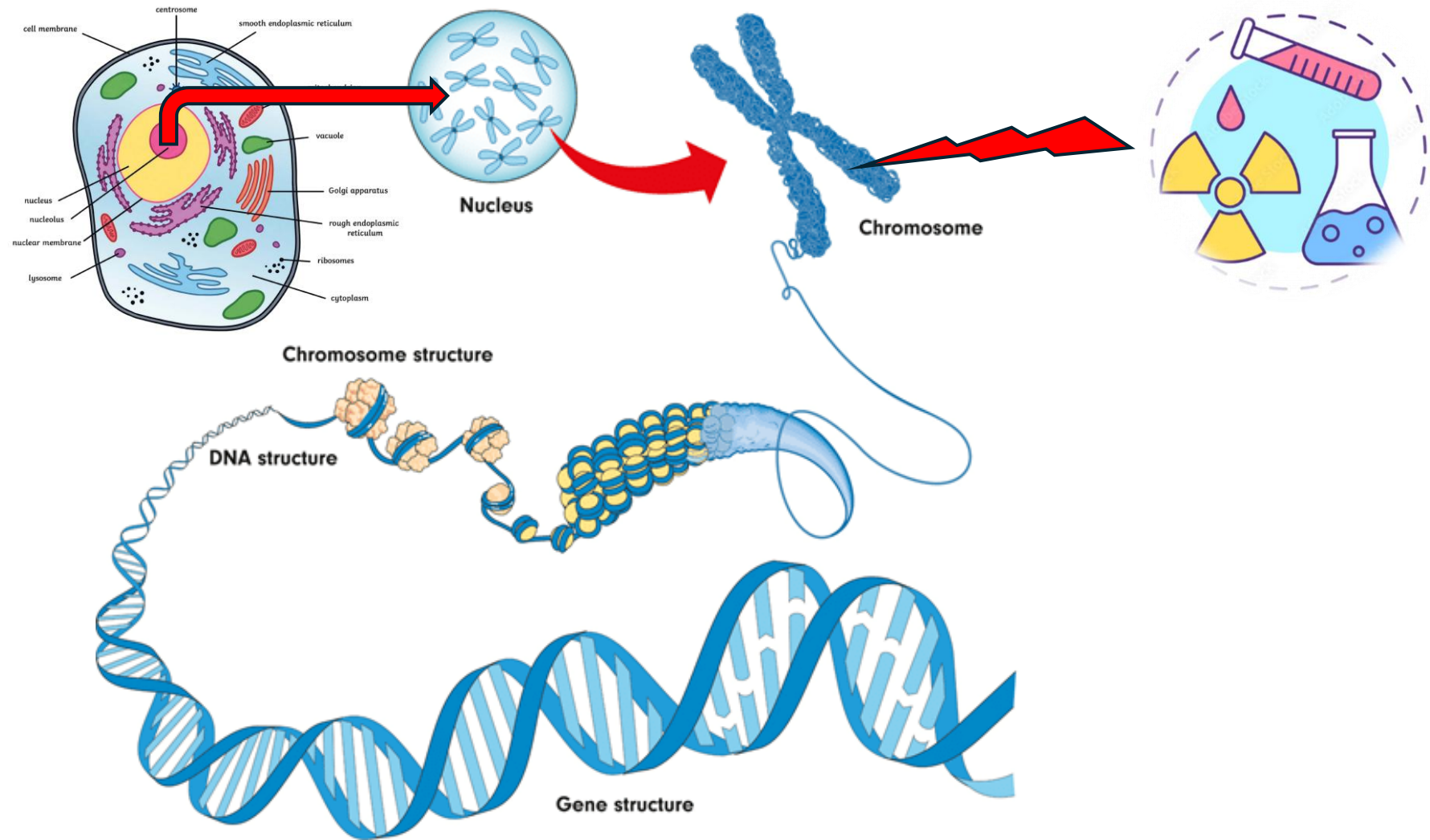
- Systemic toxicity

- ✓ Acute toxicity
- ✓ Toxicokinetics
- ✓ Genotoxicity
 - ❖ Mutagenicity
 - ❖ Chromosomal damage
- ✓ Repeated dose toxicity
 - Subacute (28d)
 - Subchronic (90d)
 - Chronic (85% of life)
- ✓ Reproductive toxicity
- ✓ Developmental Toxicity
- ✓ Carcinogenicity

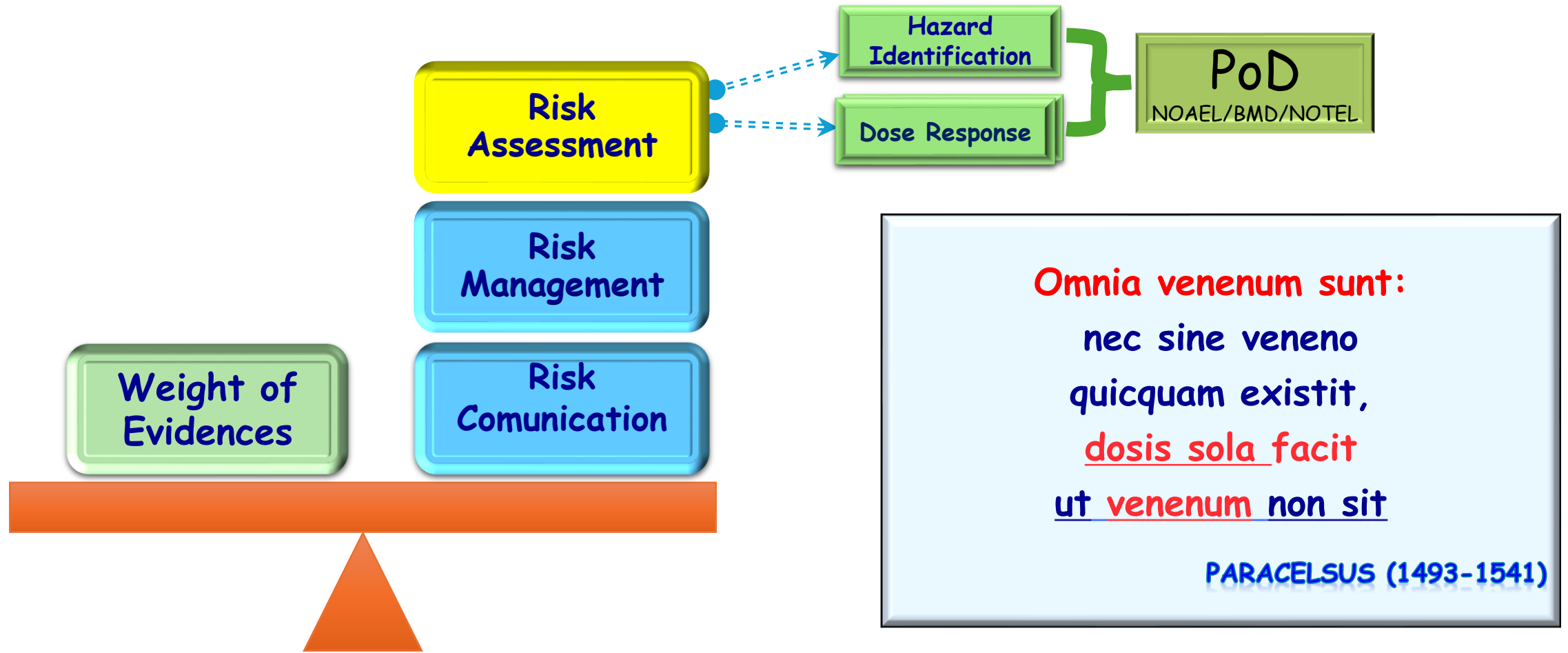
TOXICOKINETICS



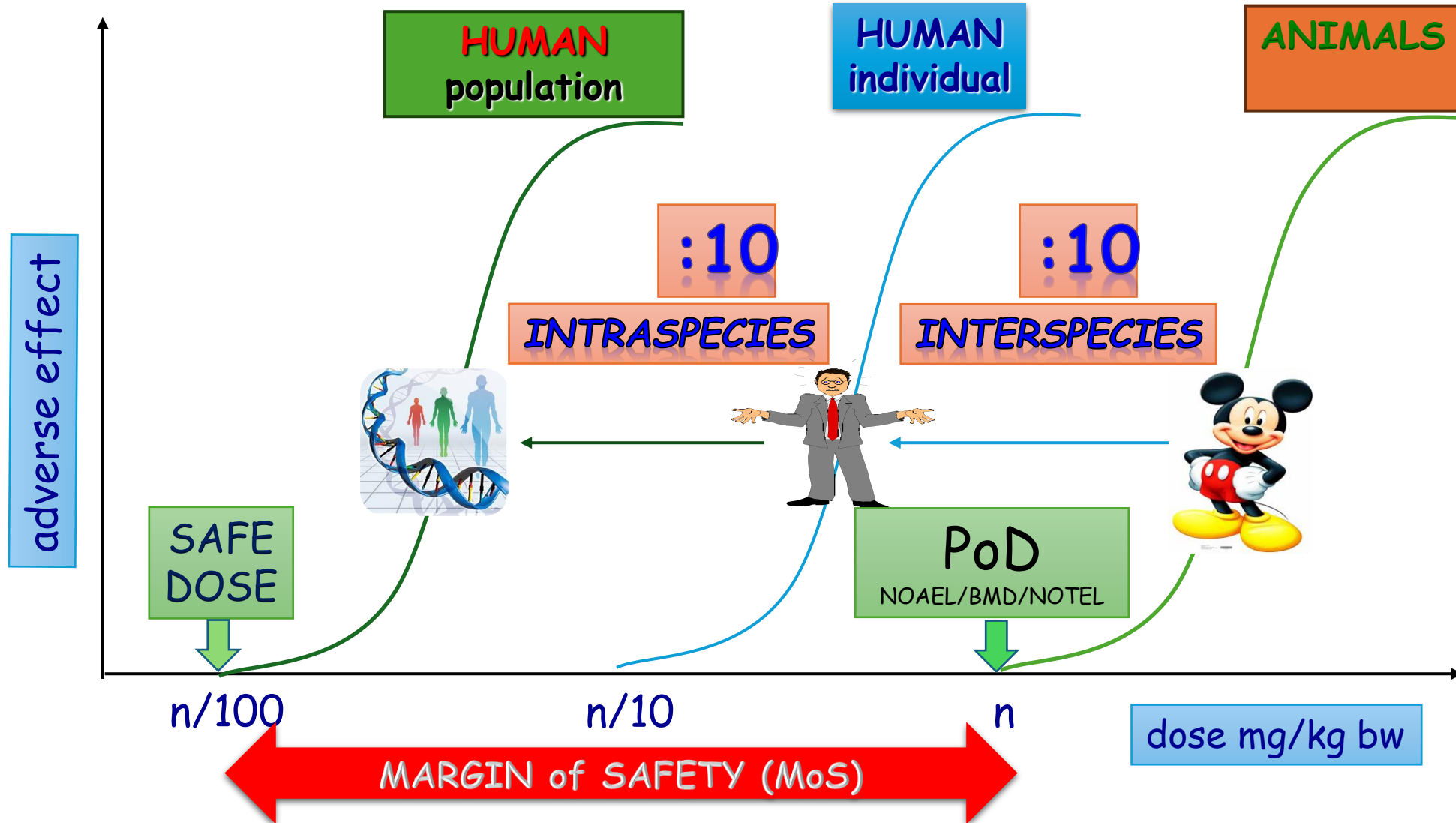
TARGET



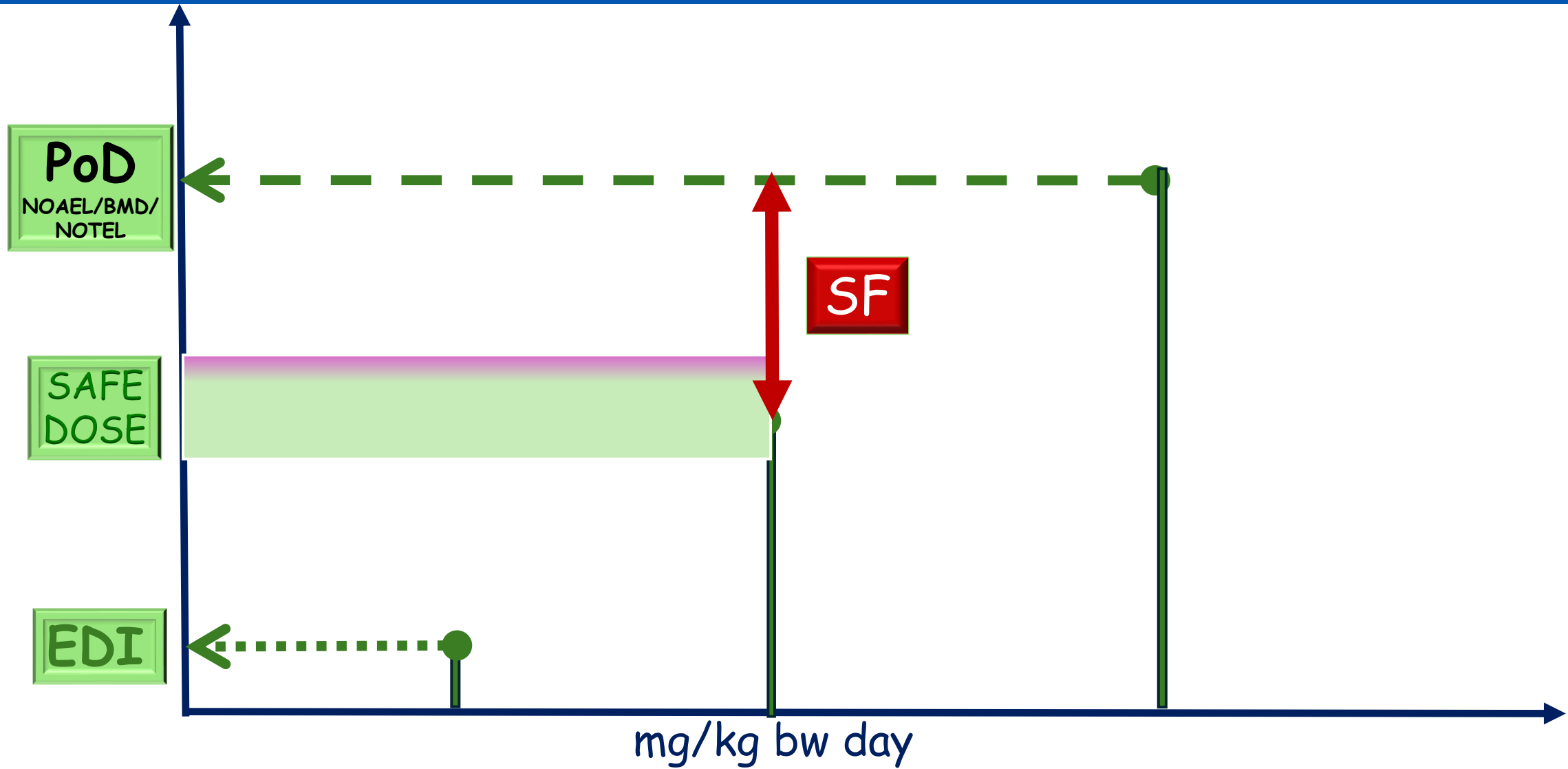
RISK ANALYSIS PARADIGM



SAFETY ASSESSMENT



SAFE DOSE



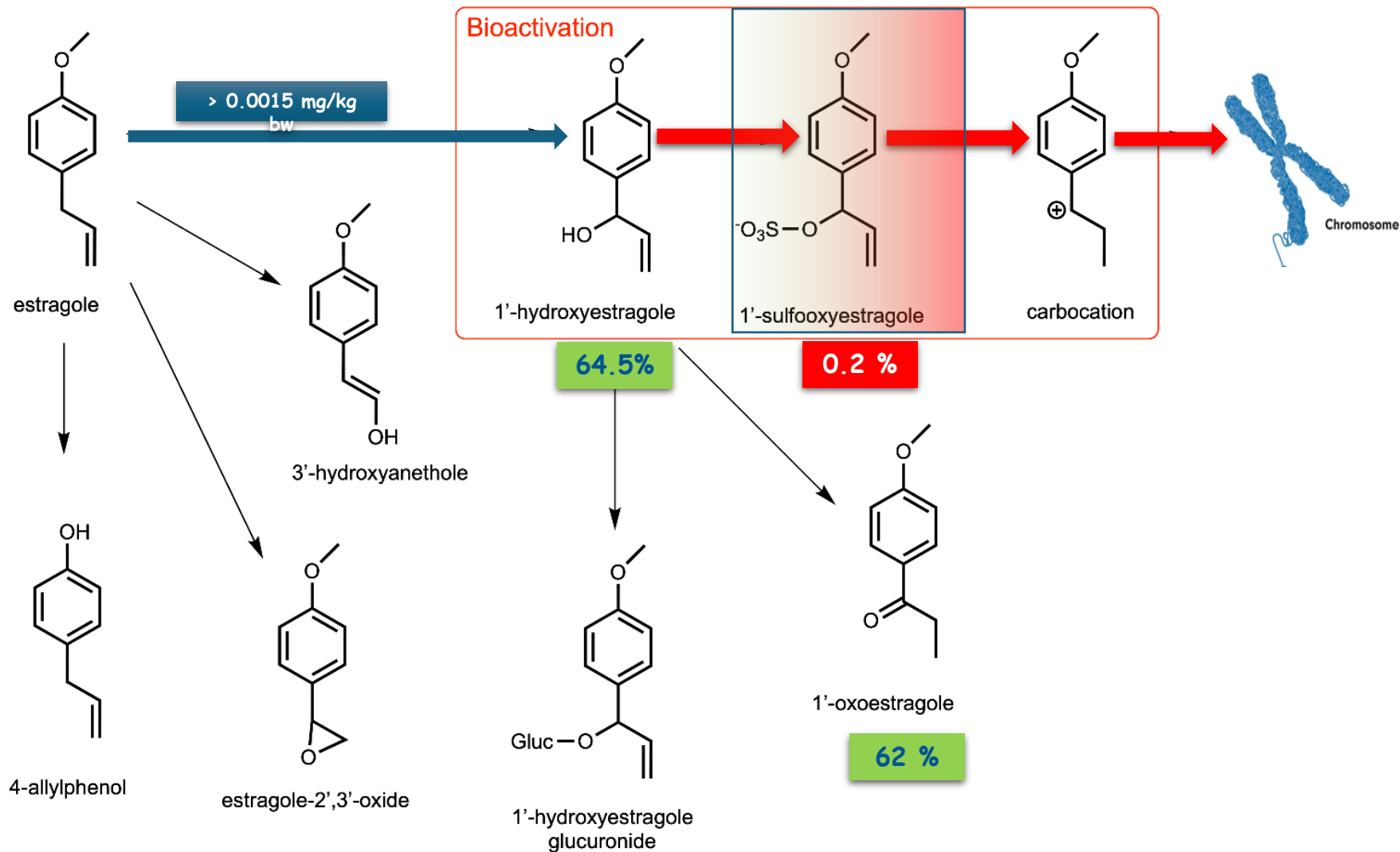
RISK ANALYSIS PARADIGM



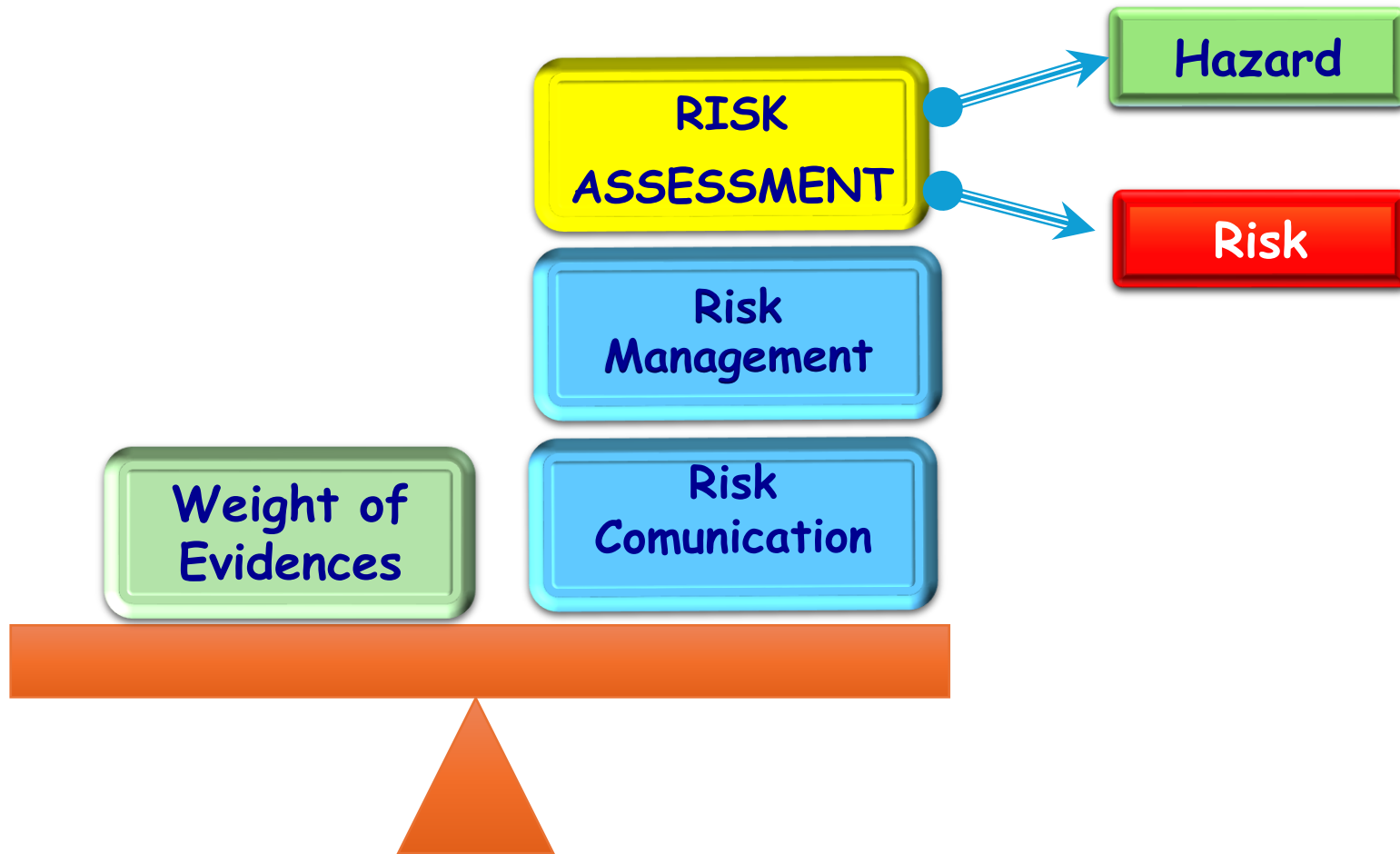
RISK ANALYSIS PARADIGM



ESTRAGOLE



HAZARD vs RISK

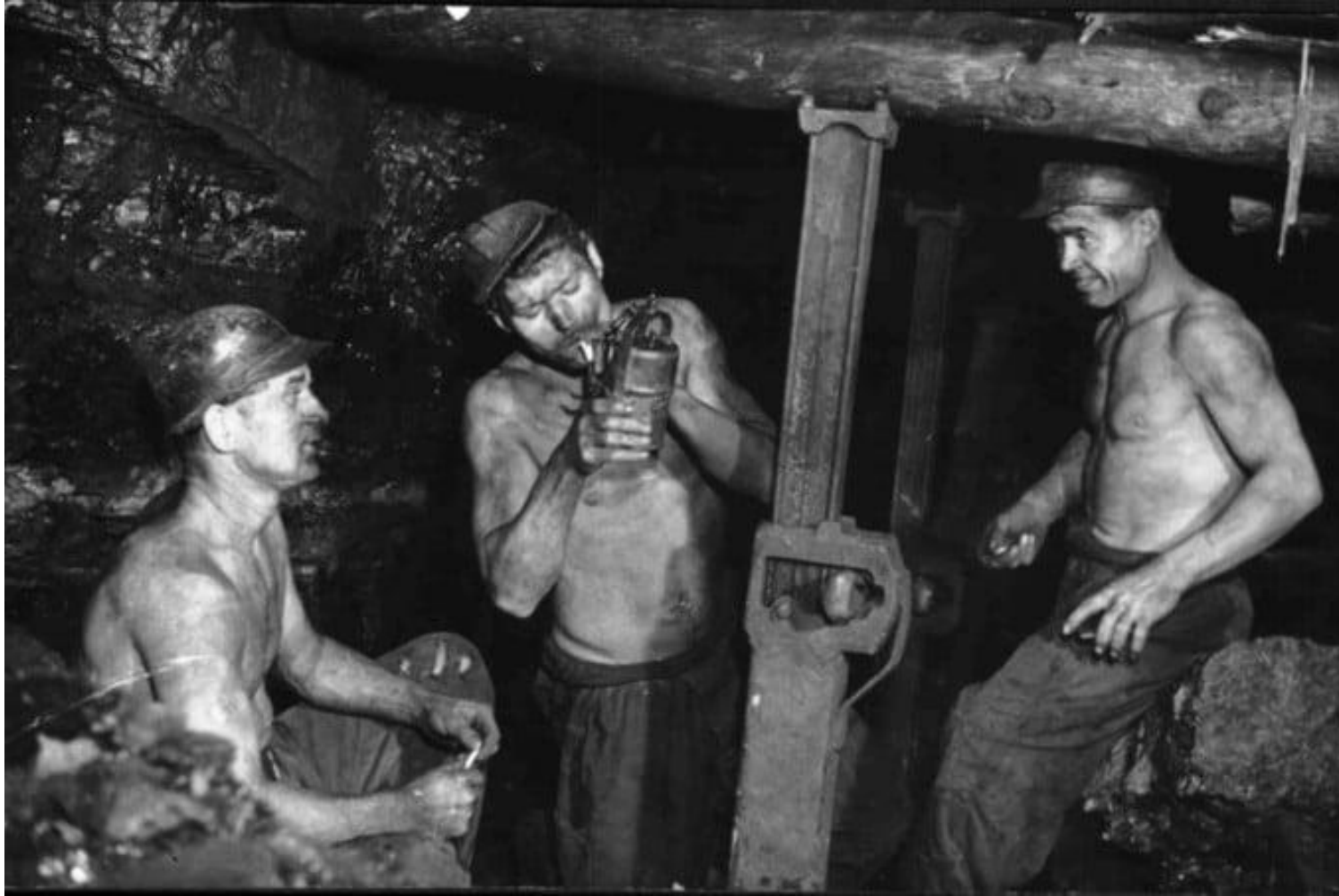


HAZARD



Hazard

RISK

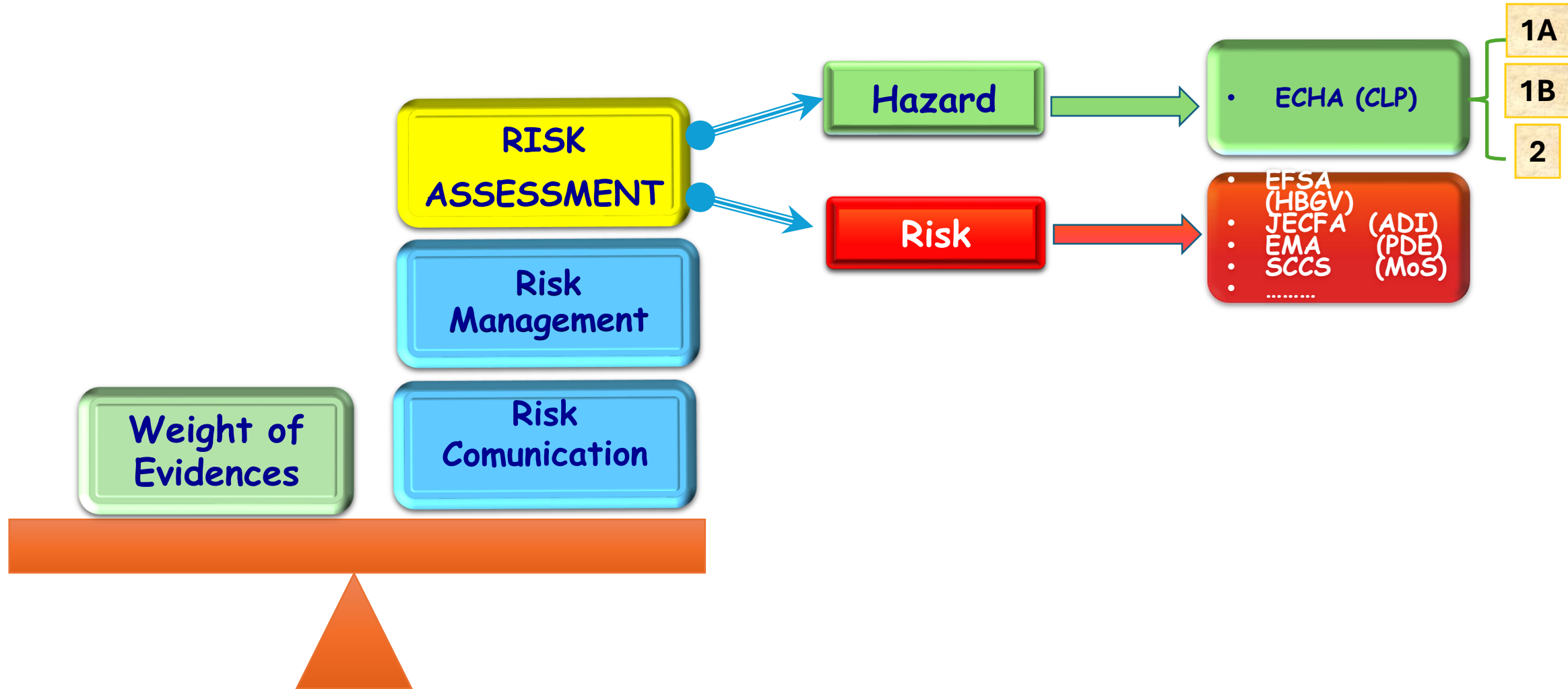


Risk

hazard

extent of exposure

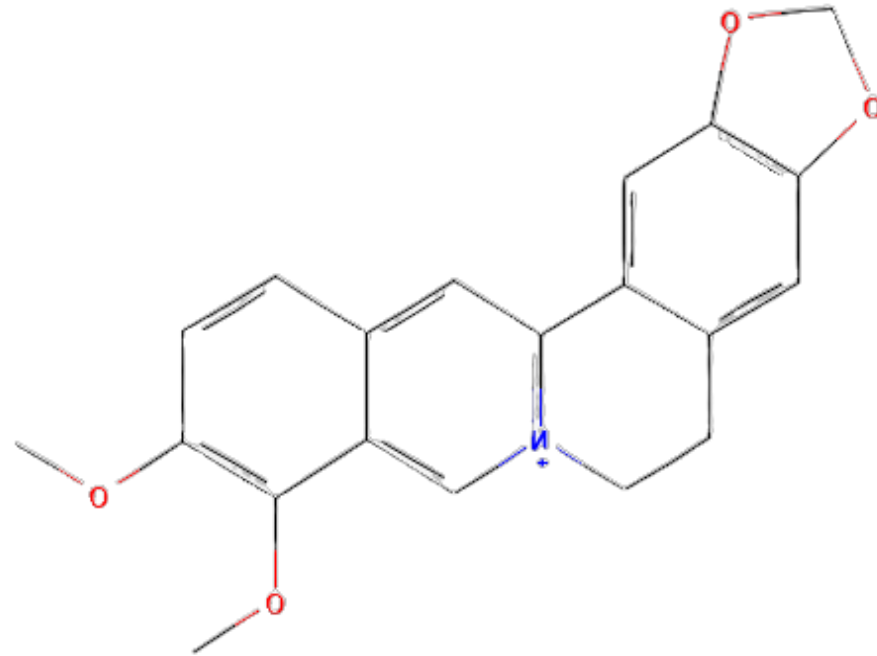
HAZARD vs RISK



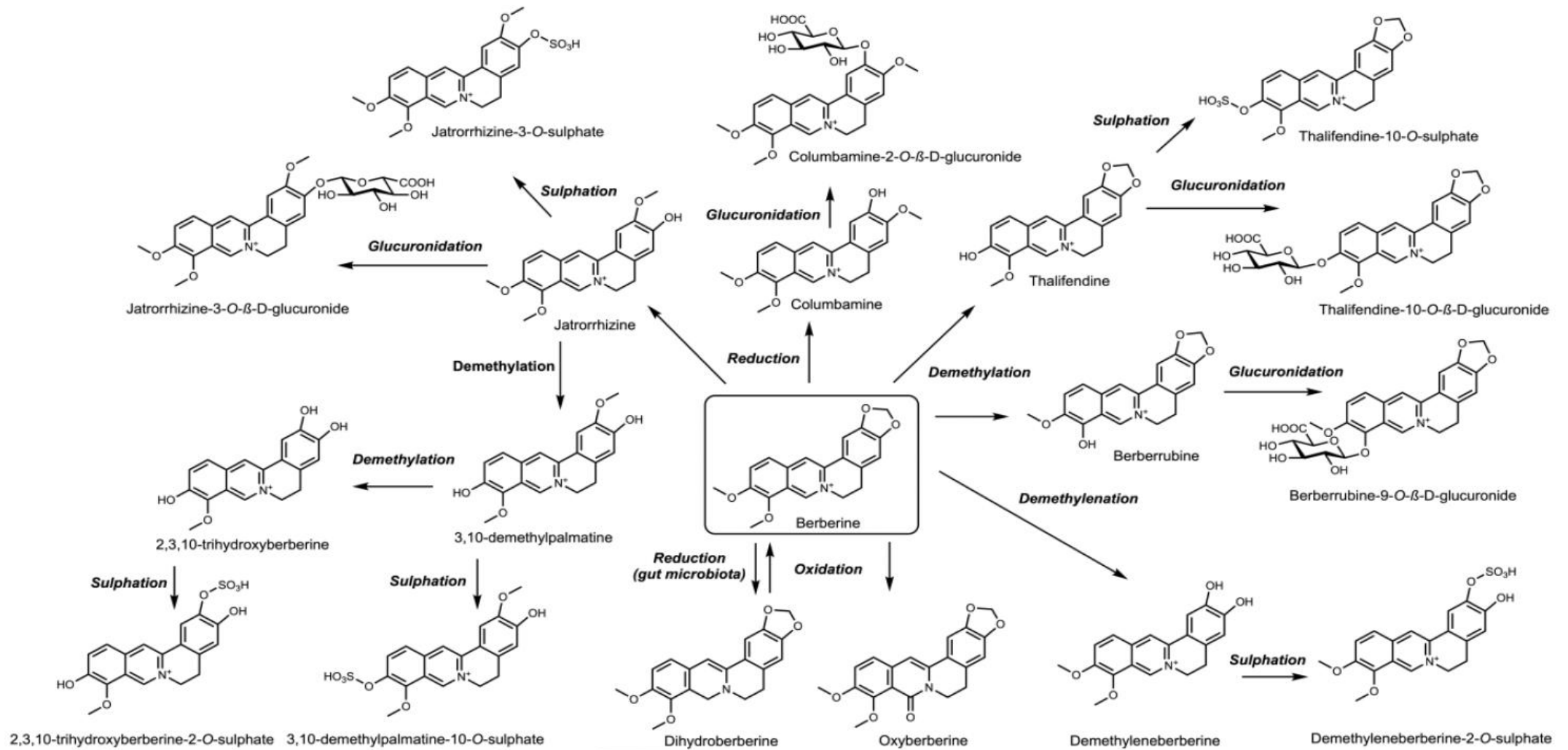
CASE STUDY

Berberine

BERBERINE



PROTOBERBERINE ALKALOIDS



DRAFT - Panel on Nutrition, Novel Foods and Food Allergens (2025)

Scientific Opinion on the safety of plant preparations containing berberine EFSA-Q-2022-00803.

PLANT SPECIES

Table 1: Plant species and their parts included in the assessment

Scientific name ^a	Plant part in the mandate	Common names ^{a, b}
<i>Berberis aquifolium</i> Pursh	Root	Oregon grape; holly-leaved barberry
<i>Berberis aristata</i> DC.	Root, bark	Indian barberry
<i>Berberis vulgaris</i> L.	Root, bark	Common barberry
<i>Chelidonium majus</i> L.	Herb	Greater celandine
<i>Coptis japonica</i> (Thunb.) Makino	Rhizome	Japanese goldthread
<i>Coptis teeta</i> Wall.	Rhizome	Indian goldthread
<i>Coptis trifolia</i> (L.) Salisb.	Rhizome	Three-leaf goldthread; savoyane
<i>Coscinonium fenestratum</i> (Goetgh.) Colebr.	Root, stem	Tree turmeric; false calumba
<i>Hydrastis canadensis</i> L.	Rhizome	Goldenseal; orange root; eye-balm
<i>Jateorhiza palmata</i> (Lam.) Miers	Root	Calumba
<i>Phellodendron amurense</i> Rupr.	Bark	Amur cork tree
<i>Thalictrum flavum</i> L.	Root	Common meadow-rue
<i>Tinospora sinensis</i> (Lour.) Merr.	Root, stem, leaf	Chinese tinospora

(a): Source: Plants of the World Online (<https://powo.science.kew.org>).

(b): Some common plant names are used for multiple plant species, therefore some of the common names listed may refer to different plant species depending on context or region.

PLANT SPECIES

Table 1: Plant species and their parts included in the assessment

Scientific name ^a	Plant part in the mandate	Common names ^{a, b}
<i>Berberis aquifolium</i> Pursh	Root	Oregon grape; holly-leaved barberry
<i>Berberis aristata</i> DC.	Root, bark	Indian barberry
<i>Berberis vulgaris</i> L.	Root, bark	Common barberry
<i>Chelidonium majus</i> L.	Herb	Greater celandine
<i>Coptis japonica</i> (Thunb.) Makino	Rhizome	Japanese goldthread
<i>Coptis teeta</i> Wall.	Rhizome	Indian goldthread
<i>Coptis trifolia</i> (L.) Salisb.	Rhizome	Three-leaf goldthread; savoyane
<i>Coscinonium fenestratum</i> (Goetgh.) Colebr.	Root, stem	Tree turmeric; false calumba
<i>Hydrastis canadensis</i> L.	Rhizome	Goldenseal; orange root; eye-balm
<i>Jateorhiza palmata</i> (Lam.) Miers	Root	Calumba
<i>Phellodendron amurense</i> Rupr.	Bark	Amur cork tree
<i>Thalictrum flavum</i> L.	Root	Common meadow-rue
<i>Tinospora sinensis</i> (Lour.) Merr.	Root, stem, leaf	Chinese tinospora

(a): Source: Plants of the World Online (<https://powo.science.kew.org>).

(b): Some common plant names are used for multiple plant species, therefore some of the common names listed may refer to different plant species depending on context or region.

EFSA REQUESTS

- i. Evidence of adverse effects of berberine as a single substance;
- ii. Evidence of adverse effects of other alkaloids of the same family as berberine (protoberberine alkaloids), given their high structural similarity with berberine and their co- occurrence in plant species;
- iii. Evidence of adverse effects of the whole preparations of the respective plant species, and relevant parts thereof.

Step 1 Characterisation

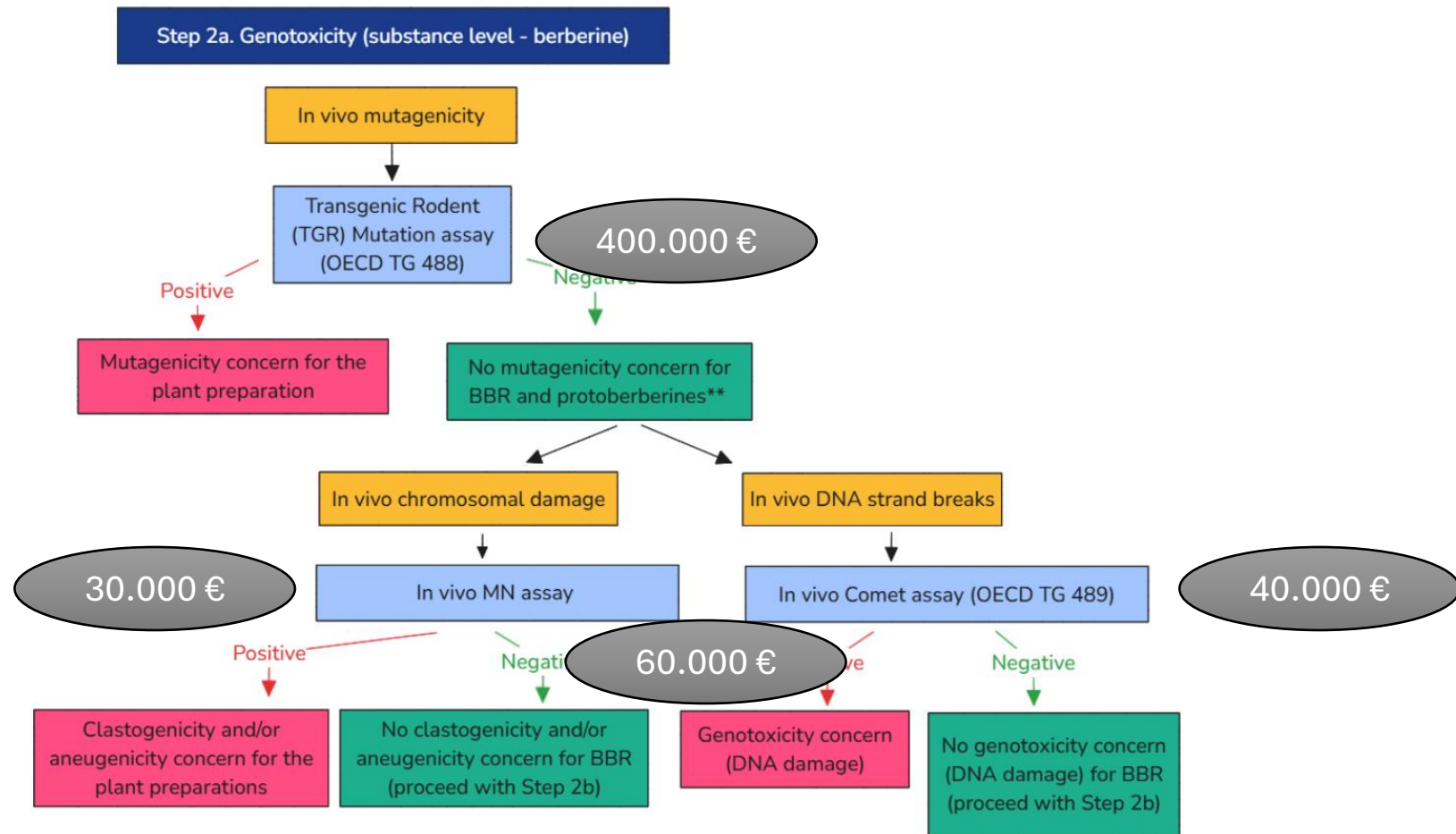
Step 2a Genotoxicity of berberine

Step 2b Genotoxicity of other protoberberines

Step 3 Genotoxicity of the plant preparations

Step 4 Subchronic toxicity study and other studies, in case genotoxicity is ruled out

EFSA REQUESTS



**Step 2 (mixture level) in accordance with EFSA GD on genotoxicity testing strategy (EFSA SC, 2011) and EFSA GD on genotoxicity assessment of chemical mixtures (EFSA SC, 2019)*

***For mutagenicity as the endpoint, read-across from berberine to the entire protoberberine family is possible*

EFSA REQUESTS

- ❖ Evidence of adverse effects of berberine as a single substance;
- ❖ Evidence of adverse effects of other alkaloids of the same family as berberine (protoberberine alkaloids), given their high structural similarity with berberine and their co- occurrence in plant species;
- ❖ Evidence of adverse effects of the whole preparations of the respective plant species, and relevant parts thereof.

Step 1 Characterisation

Step 2a Genotoxicity of berberine 60.000 €

Step 2b Genotoxicity of other protoberberines

Step 3 Genotoxicity of the plant preparations

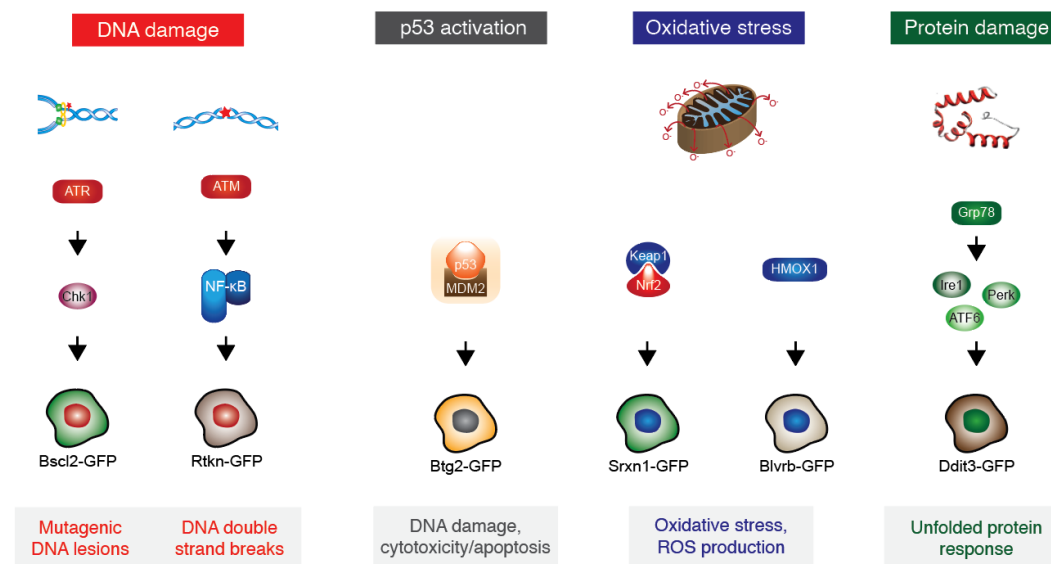
Step 4 Subchronic toxicity study and other studies, in case genotoxicity is ruled out

250.000 €

FBR UNDERTAKING

Item Description	Product code	No. of tests	Price per test (€)	Total (€)*
ToxTracker Analysis	8000	1	€ 5,850	€ 5,850
Total				€ 5,850

*Excludes VAT. Contracting through third-party platforms may require price adjustments.



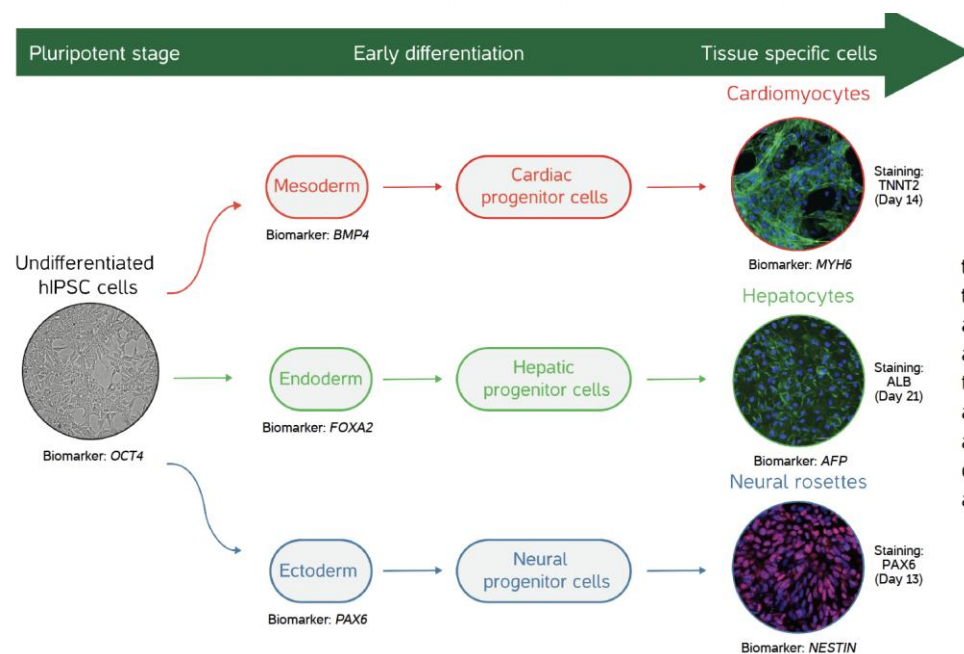
FBR UNDERTAKING

Description of analysis	Product code	No. of tests	Price per compound	Total*
ReproTracker analysis	8012	1	€ 22,650	€ 22,650

TOTAL

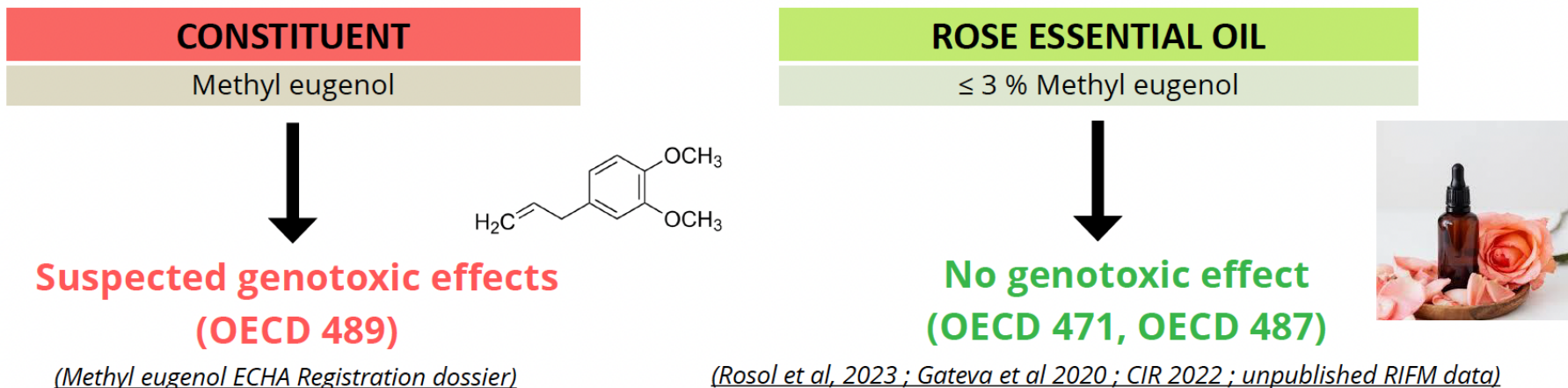
€ 22,650

*Excludes VAT. Contracting through a third-party platform may require price adjustments, final pricing may be modified accordingly.



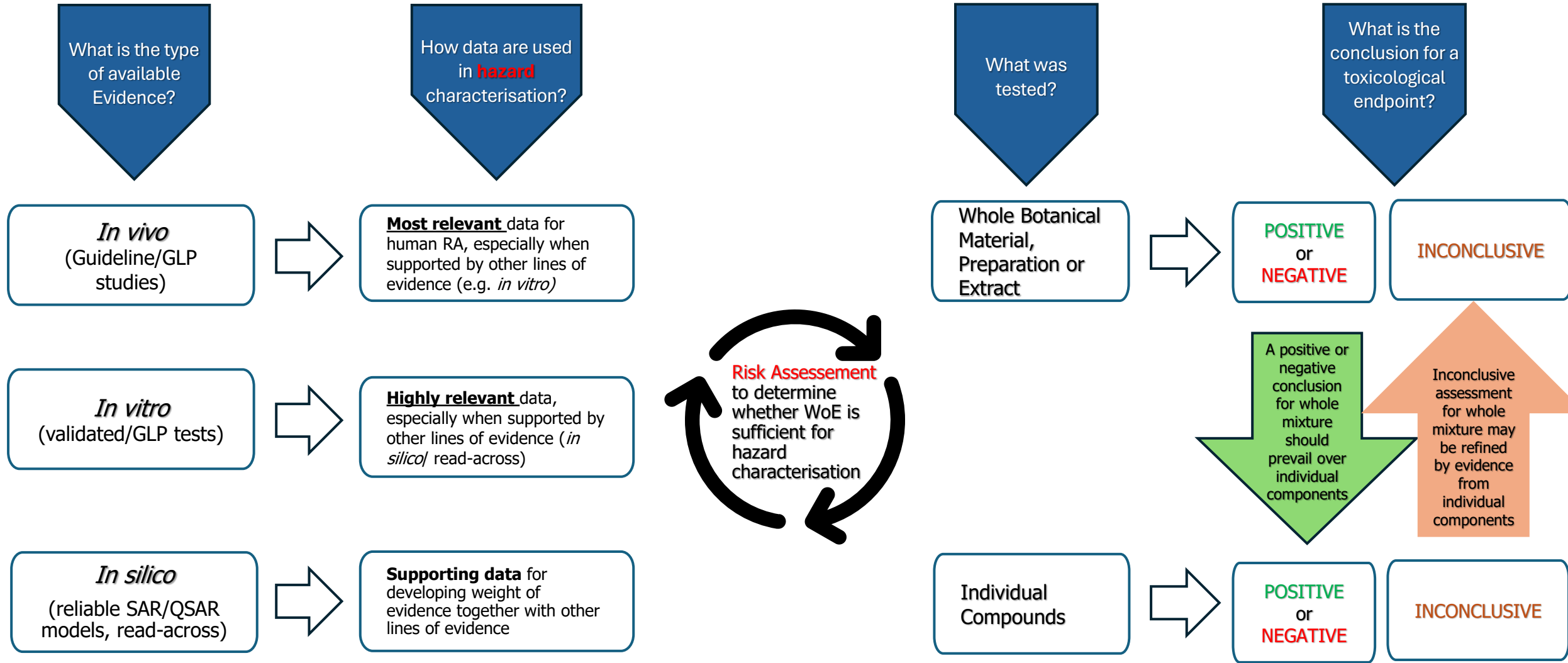
Scientific Evidence #2

COMPARISON CONSTITUENT VS EO:



**BASED ON METHYL EUGENOL CONTENT, ROSE EO WOULD BE CLASSIFIED CMR2 WHILE DATA
(OECD tests) SHOW NO EFFECT**

Weight of Evidence Approach for Hazard Assessment of Botanical Materials, Preparations and Extracts



THANK YOU

prof. **Corrado L. Galli**

Laboratory of Toxicology and Risk Assessment

Department of Pharmacological and Biomolecular Sciences "Rodolfo Paoletti"

Università degli Studi di Milano

via Balzaretti 9, 20133 Milano

Tel +39 3356025209

corradolodovico.galli@gmail.com

corrado.galli@unimi.it