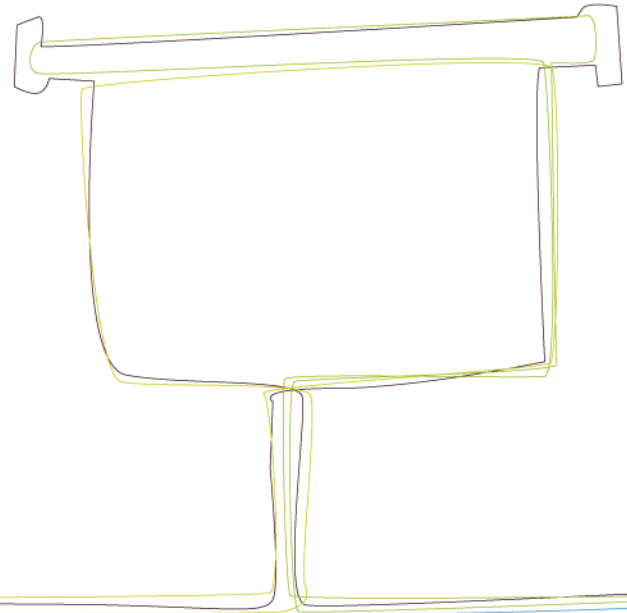


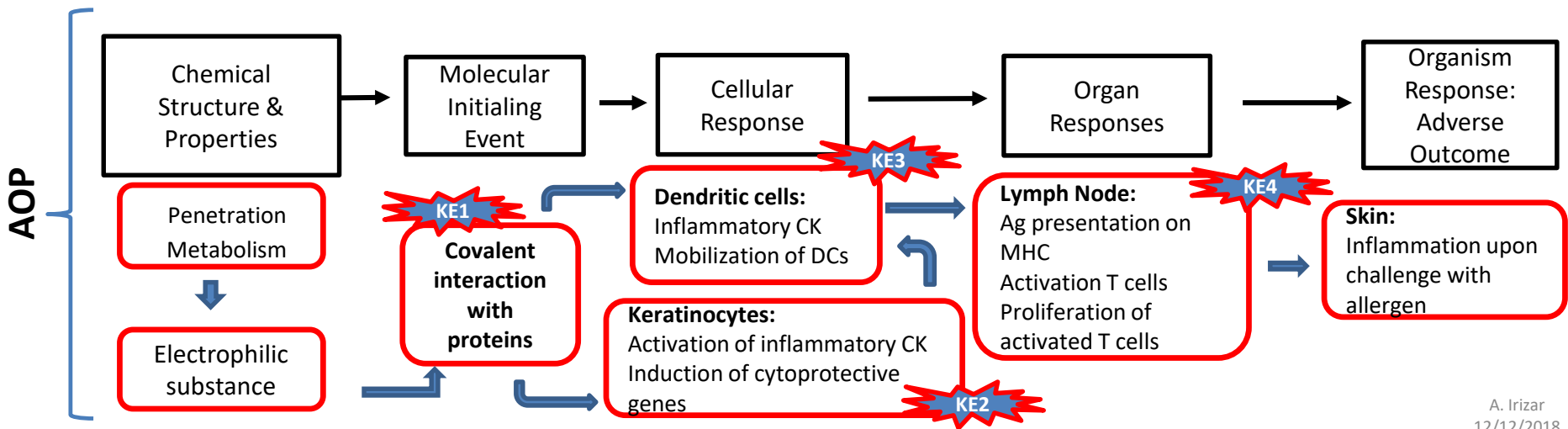


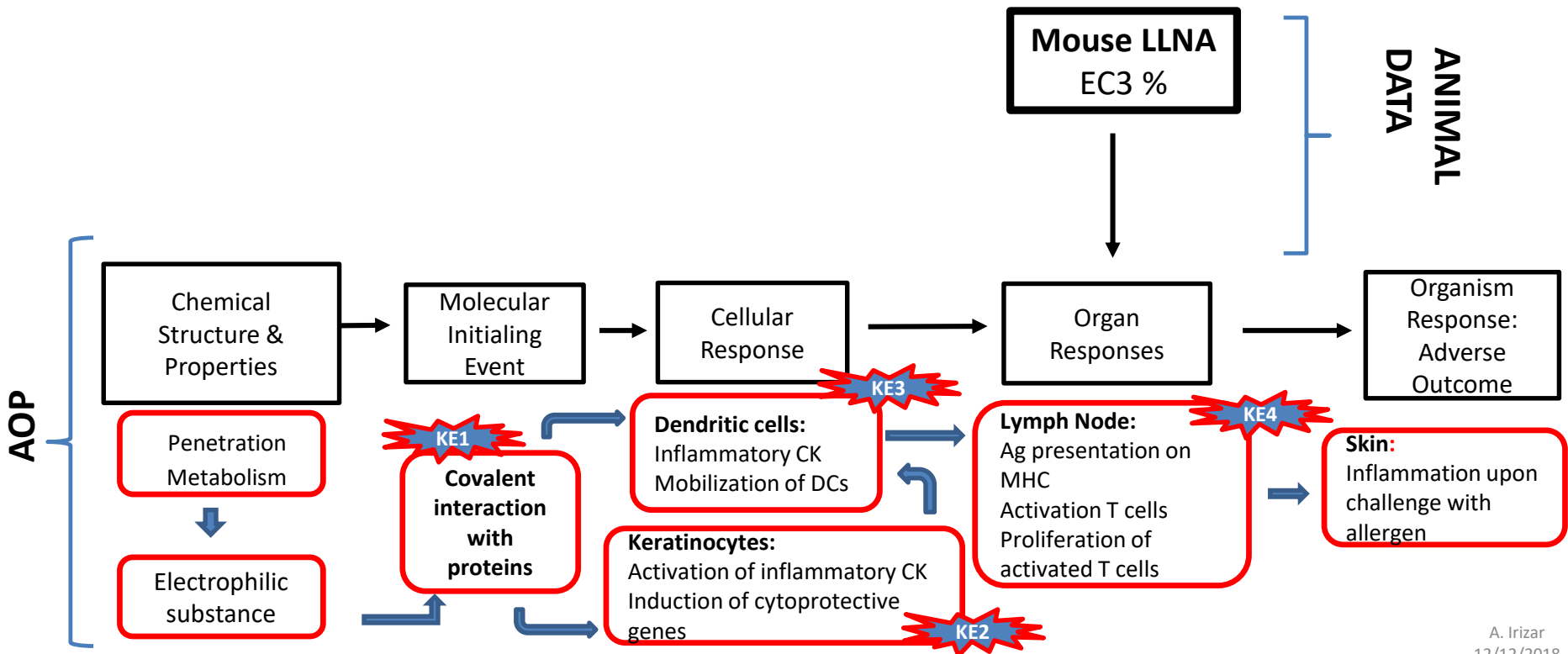
Setting the scene: skin sensitization AoP and current AAT methods

IDEA Workshop on the
Characterisation and Categorisation of Allergens

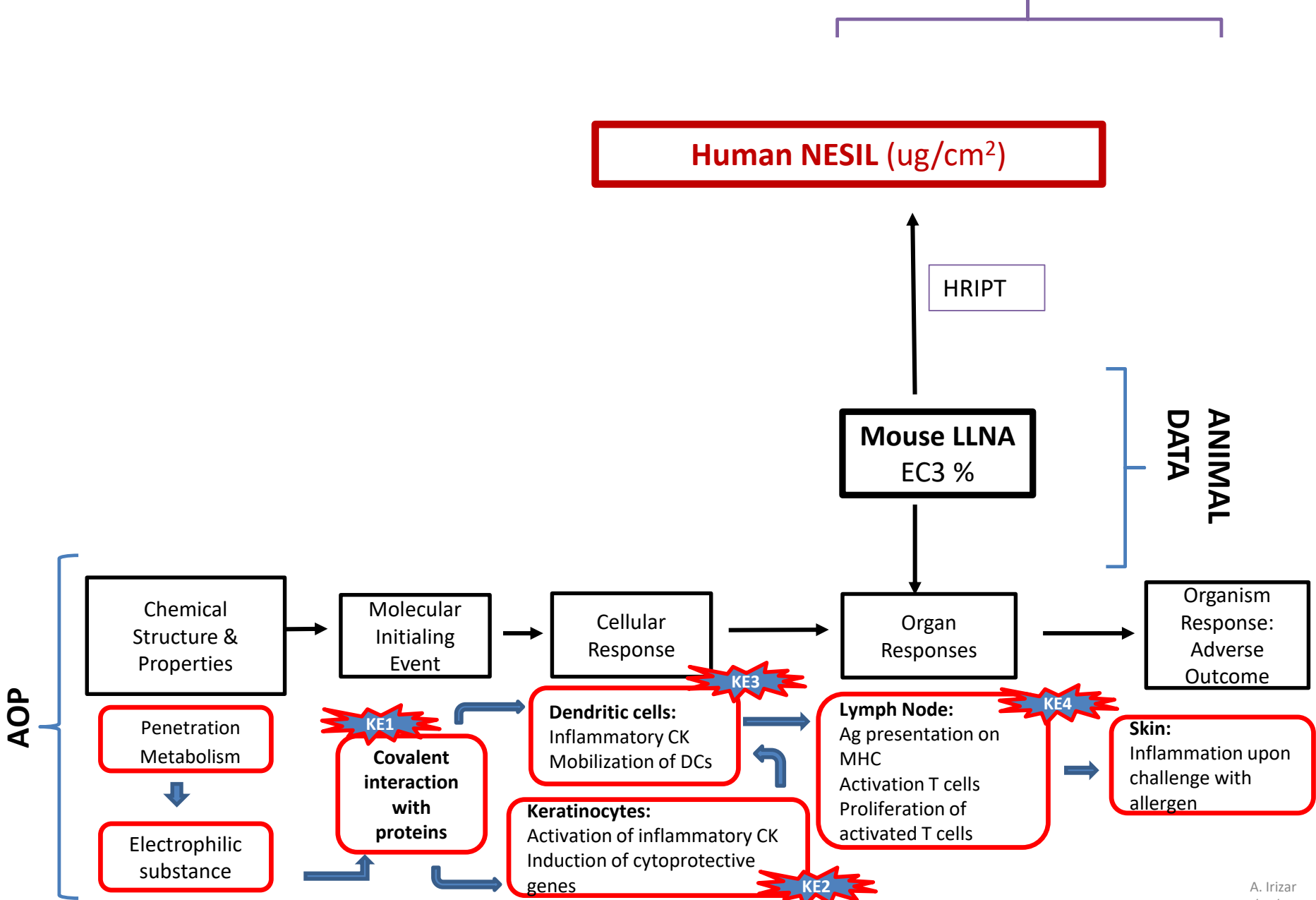
Amaia Irizar
12th December 2018







CURRENT QRA



CURRENT QRA

Human NESIL (ug/cm²)

HRIPT

Data Interpretation Procedures: Ruled-based, Mathematical and Machine Learning Models

NA DATA

AOP

ANIMAL DATA

In silico

In chemico

In vitro

Chemical Structure & Properties

Molecular Initiating Event

Cellular Response

Organ Responses

Organism Response: Adverse Outcome

Penetration Metabolism

Electrophilic substance

Covalent interaction with proteins

Dendritic cells: Inflammatory CK Mobilization of DCs

Keratinocytes: Activation of inflammatory CK Induction of cytoprotective genes

Lymph Node: Ag presentation on MHC Activation T cells Proliferation of activated T cells

Skin: Inflammation upon challenge with allergen

KE1

KE3

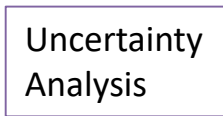
KE2

KE4

NON-ANIMAL QRA

CURRENT QRA

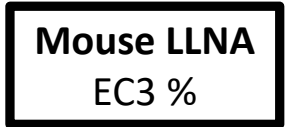
Other Data WoE Exposure



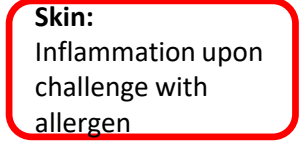
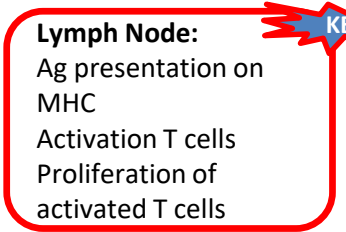
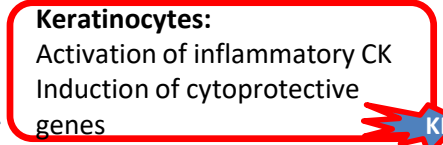
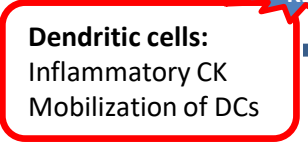
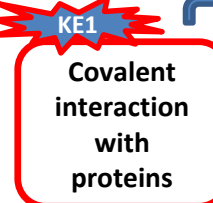
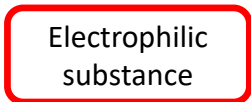
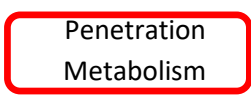
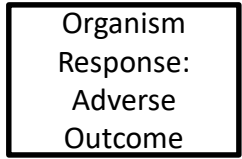
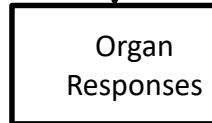
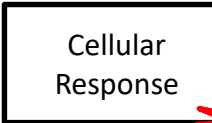
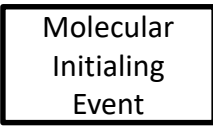
Data Interpretation Procedures: Ruled-based, Mathematical and Machine Learning Models

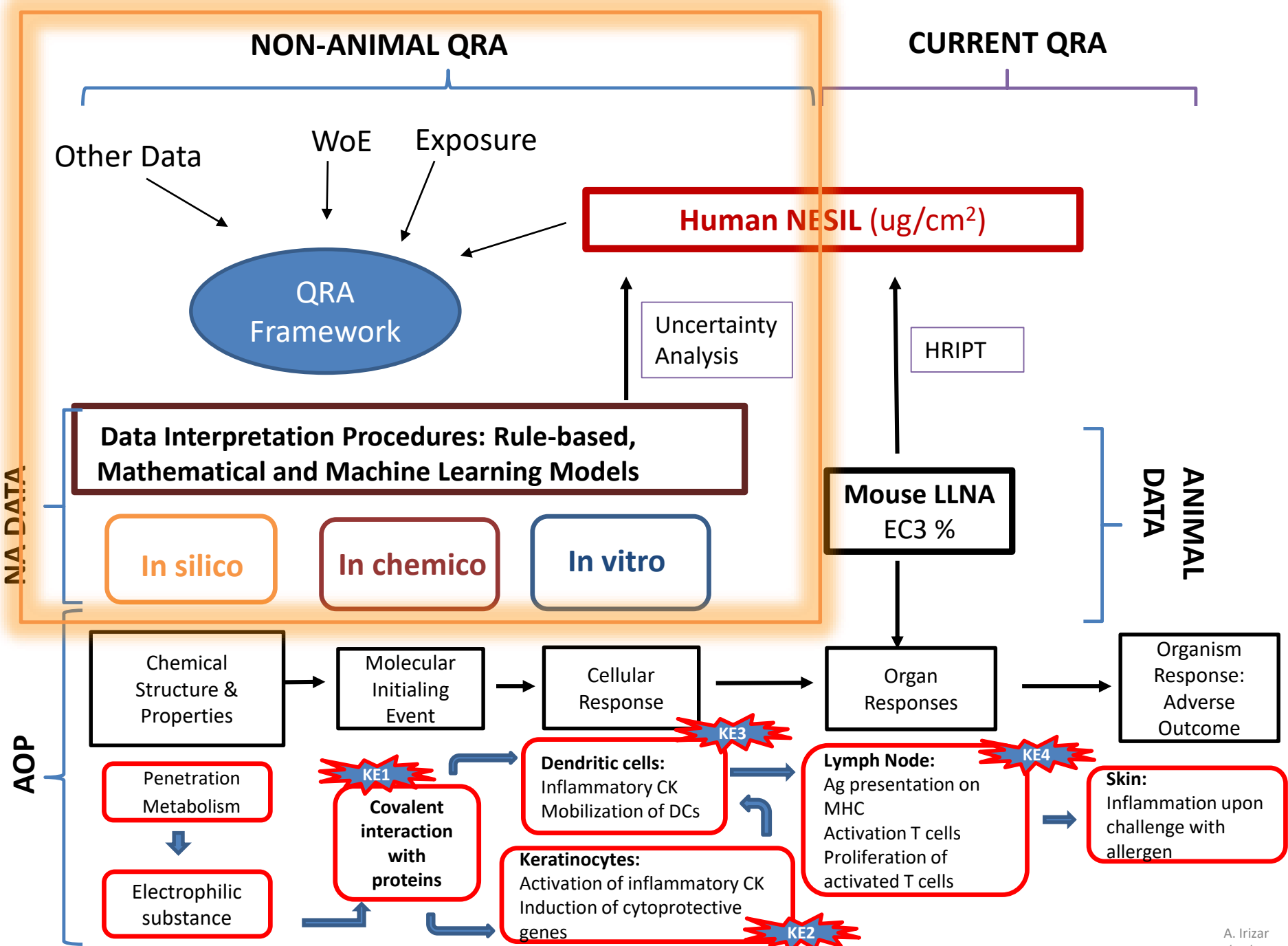
NA DATA

ANIMAL DATA



AOP





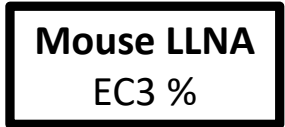
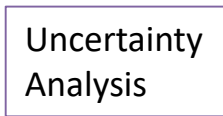
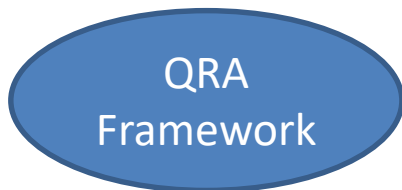
NON-ANIMAL QRA

CURRENT QRA

Other Data

WoE

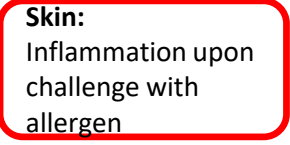
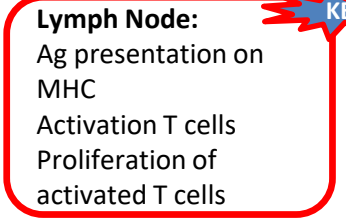
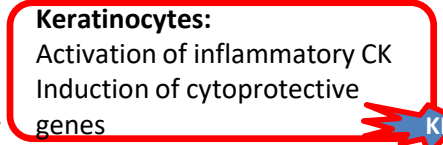
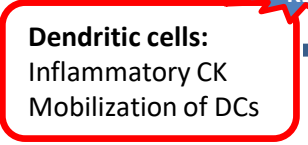
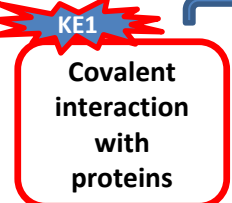
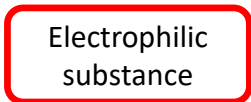
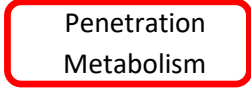
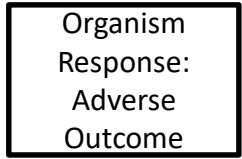
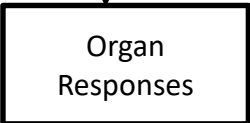
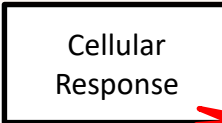
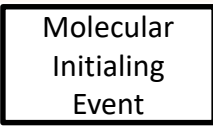
Exposure



ANIMAL DATA

NA DATA

AOP



KE3

KE1

KE2

KE4

OECD Test guideline available

OECD Test guideline available

In the OECD Work Plan

OECD Test guideline available

In the OECD Work Plan

**Some validation done/in
progress/Commercialised**

OECD Test guideline available

In the OECD Work Plan

**Some validation done/in
progress/Commercialised**

Not validated/Not commercialised

In Silico

In Silico

Derek

Times SS

OECD toolbox

Case Ultra

SkinSensDB

ToxTree

VEGA

Topkat

REACHAcross

MuDRA

In Silico

In Chemico

Derek

Times SS

OECD toolbox

Case Ultra

SkinSensDB

ToxTree

VEGA

Topkat

REACHAcross

MuDRA

In Silico

In Chemico

Derek

DPRA (KE1)

Times SS

ADRA (KE1)

OECD toolbox

kDPRA (KE1)

Case Ultra

PPRA (KE1)

SkinSensDB

EASA (KE1)

ToxTree

VEGA

Topkat

REACHAcross

MuDRA

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DPRA (KE1)

Times SS

ADRA (KE1)

OECD toolbox

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SkinSensDB

EASA (KE1)

ToxTree

VEGA

Topkat

REACHAcross

MuDRA

In Silico

In Chemico

In Vitro

Derek

DPRA (KE1)

KeratinoSens
(KE1?/KE2)

hCLAT (KE3)

IL-1 β Luc assay
(KE3)

Times SS

ADRA (KE1)

LuSens (KE1?/KE2)

IL-8 Luc assay (KE3)

IL-2 Luc assay (KE3)

OECD toolbox

kDPRA (KE1)

SENS-IS (3D) (KE2)

U-SENS (KE3)

Vitrigel-SST(KE3)

Case Ultra

PPRA (KE1)

ARE c32 (KE1?/KE2)

GARDskin (KE3)

Cocat (KE2/KE3)

SkinSensDB

EASA (KE1)

SenCeeTox (3D)
(KE1?/KE2)

m-MUSST (KE3)

PBMDC (KE3)

ToxTree

IL-18 (3D) (KE2)

Skimune (KE?)

VITOLENS (KE3)

VEGA

EpiSensA (3D) (KE2)

SensiDerm (KE3)

Topkat

REACHAcross

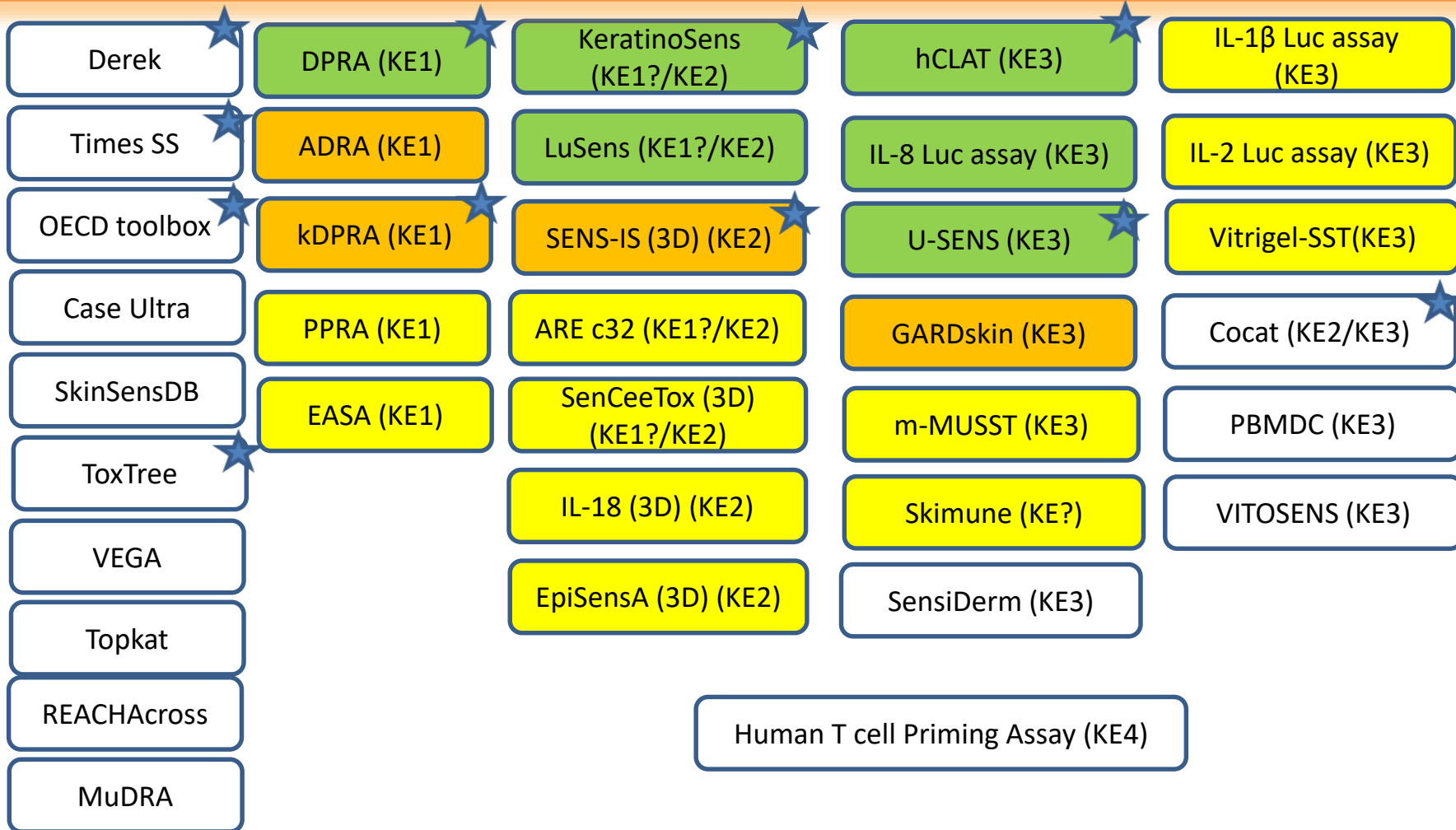
Human T cell Priming Assay (KE4)

MuDRA

In Silico

In Chemico

In Vitro



Conclusion



- A plethora of methods are developed to address the different KE of the AOP
- These are at different level of validation, commercialization and regulatory acceptance
- Some fixed data interpretation procedures (DIP) are starting to be evaluated at OECD level
- A combination of these methods together with DIP and other elements within an IATA is used to predict quantitative potency
- **Further exploration of the underlying AOP may help identify the key elements that drive and/or regulate the skin sensitization induction potency**