Part Four

AI – Use case in Toxicology applications

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Background: Read across* assessment of chemicals

Traditional way of handling a Toxicological Risk Assessment (TRA) containing data-poor chemicals (ISO 10993-17 or ISO 18562-series for volatiles)

identified data poor chemicals / group → Search for chemical analogues using structural data and other data

Use online sources to investigate / confirm scientific accuracy and stringency → Perform / author full tox risk assessment, calculate numerical risks

Include and conclude in the final TRA Report

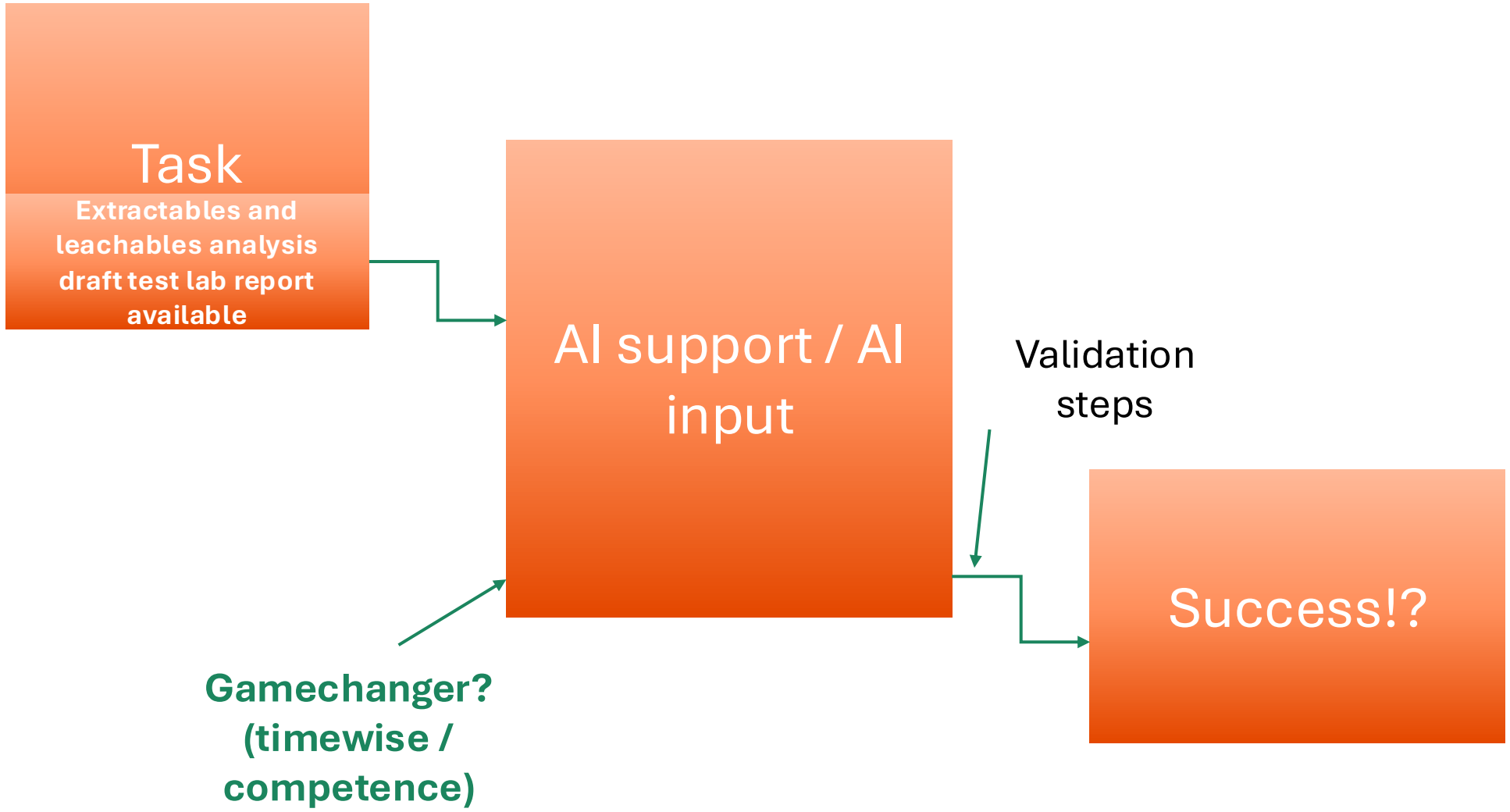
*_**"Read across"** uses existing data from closely related substances to estimate the safety and toxicity of a substance with limited data (in vivo studies). The approach is based on the assumption that structurally similar substances will show similar biological and toxicological behavior, and the surrogate structure becomes the source molecule for the critical data."_

Happy Client



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Simple as that?

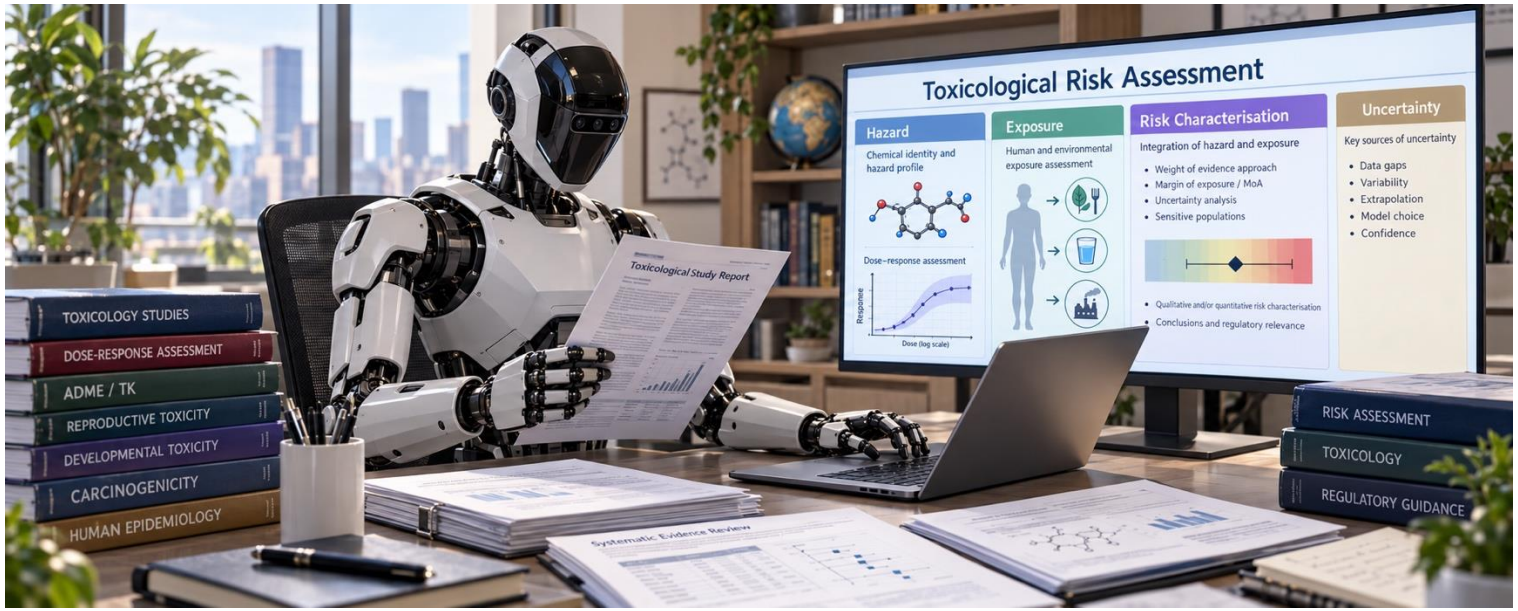


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AI - A toxicologist's best friend or worst foe, or both?

Case from the real world – diving deeper into details: benefits and potential pitfalls.

EXAMPLE: AI assisted read-across and conversation with an AI



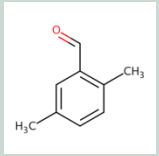
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Applied AI Toxicology - Background to the case

VOS (Inhalation, volatiles)

Aromatic Aldehyde Group

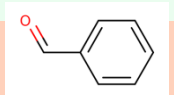
2,5-Dimethylbenzaldehyde – what do we have in terms of data?

Formula	Mw	Structure
$C_9H_{10}O$	134.178 g/mol	

Device Intended population: Up to a year, most vulnerable population: neonates.
No relevant studies found, sufficient data not located in a literature search, therefore:

Decision: Read across

Let's test what AI can do for us in this case:

AI suggested the "obvious" read across candidate: : **Benzaldehyde (CAS 100-52-7)**  - same benzaldehyde ring + aldehyde group; the two methyl substituents do not change the mode of action and tend to reduce reactivity and volatility, so the read-across is conservative – **however, no data on this either except Workers OEL without firm evidence from studies.**

Then AI and I had the following conversation:

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Cont. – conversation with AI

Carl-Johan 1: " Can you split the benzaldehyde assessment in two - the aldehyde part via acetaldehyde, the benzene ring via e.g. ethylbenzene? The aldehyde structure gives the portal-of-entry effect (nasal tissue), and systemic effects can be explored via the metabolized parent?"

AI 1: Fragment additivity (assigning the –CHO and ring substructures separate surrogate values and recombining) is rejected: toxicity is a whole-molecule property, the conjugated aryl carbonyl is not a free aliphatic carbonyl, whole-molecule metabolism does not decompose to fragment fates, and there is no validated combining rule.

In essence meaning: *You cannot estimate the toxicity of an aromatic aldehyde by separately considering the aldehyde group (–CHO) and the aromatic ring and then adding the effects together. The toxicity must be evaluated for the entire molecule because the groups interact and behave differently when they are part of the same structure.*

Carl-Johan 2: I insist

AI 2: However, the refined framing is valid and is recognized practice — endpoint-specific, mode-of-action / toxicokinetically informed read-across:

Track 1 — Local (portal of entry), CRITICAL: driven by the intact aldehyde. Anchor: benzaldehyde irritation value → ~3.5 mg/m^3 general population; acetaldehyde RfC 0.009 mg/m^3 as conservative floor.

Track 2 — Systemic, NON-LIMITING: driven by the metabolite, not the rapidly-cleared parent (benzaldehyde blood t½ ≈ 8 min → benzoic/hippuric acid). Benzoic acid is GRAS, IRIS oral RfD 4 mg/kg/day, no systemic effects ≤ 25 mg/m^3 inhalation. JECFA already sets benzaldehyde's ADI as 0–5 mg/kg bw expressed as benzoic-acid equivalents — i.e. the metabolite basis is the authoritative one. p-Tolualdehyde → p-toluic acid; 2,5-DMBA → 2,5-dimethylbenzoic acid.

The two values are not combined arithmetically: the local endpoint sets the reference value and the systemic endpoint is shown non-limiting. Ethylbenzene drops out entirely of the assessment.

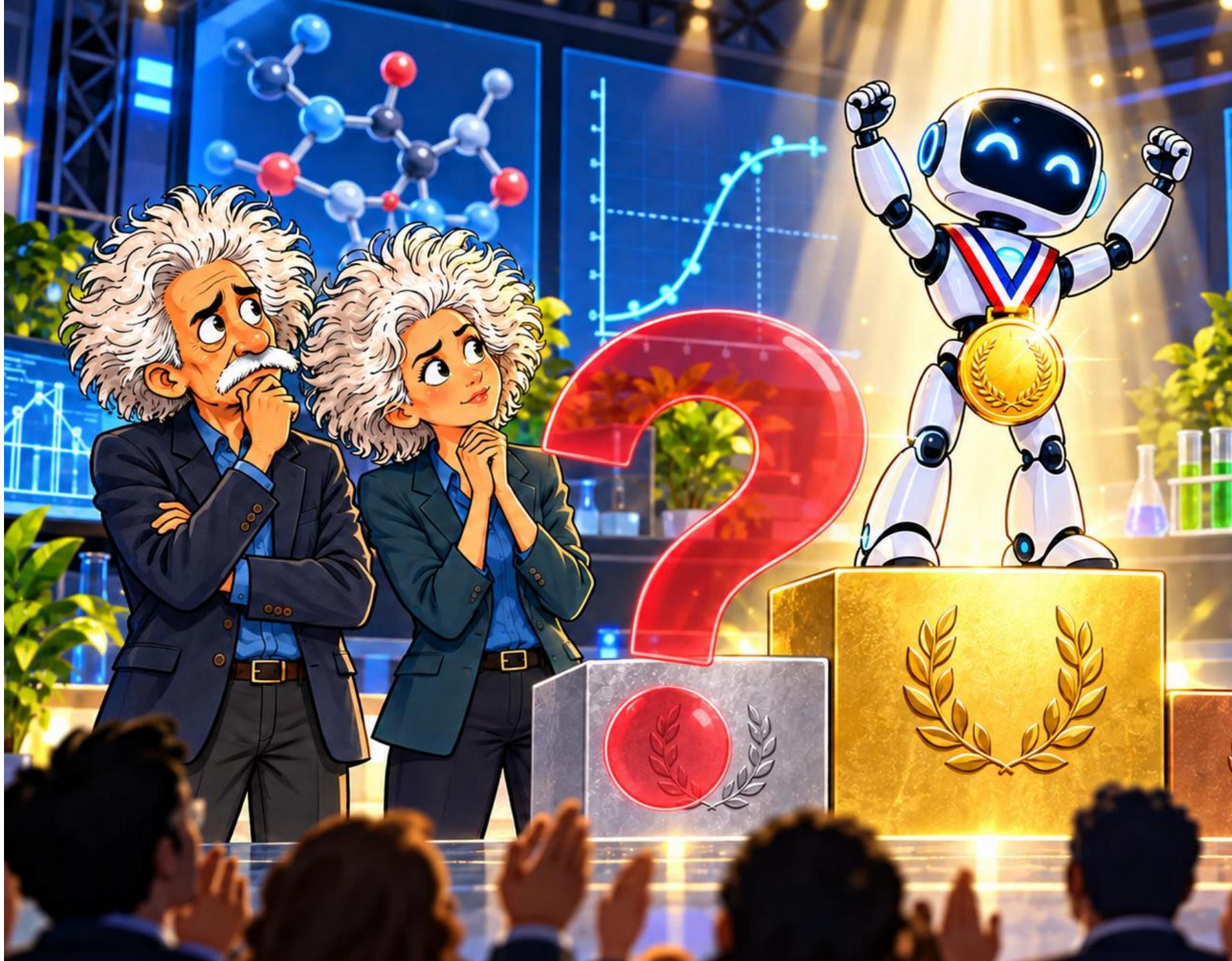
Comments, and lessons learn?

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Outcompeted?

Is AI smart?

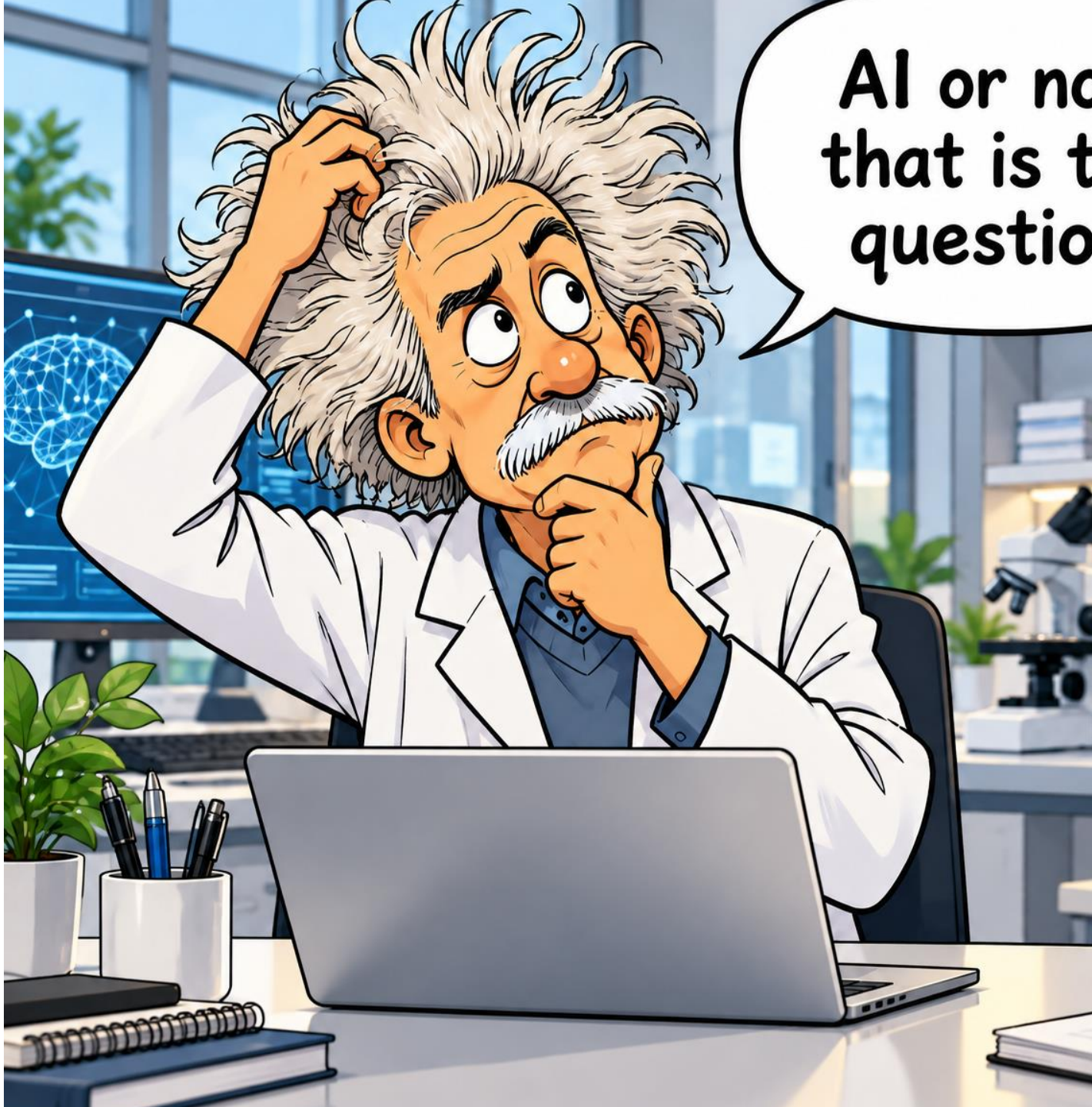
- Is often astonishingly smart, beyond most competence levels.



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Discussion

What is your / your companies view / policy with regards to using AI in the daily work tasks?



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Interactive group discussion - Q1

Are there risks of performing work / tasks beyond the competence level using AI?

Can AI help us build competence, or does it risk becoming a counterproductive shortcut?

Obvious risks?



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Interactive group discussion – Q2

Cost (€/$)-benefit, using AI in daily work tasks? Is it an issue at all?

Have you ever thought of /being informed of, the costs of using more capable AI models in your work?

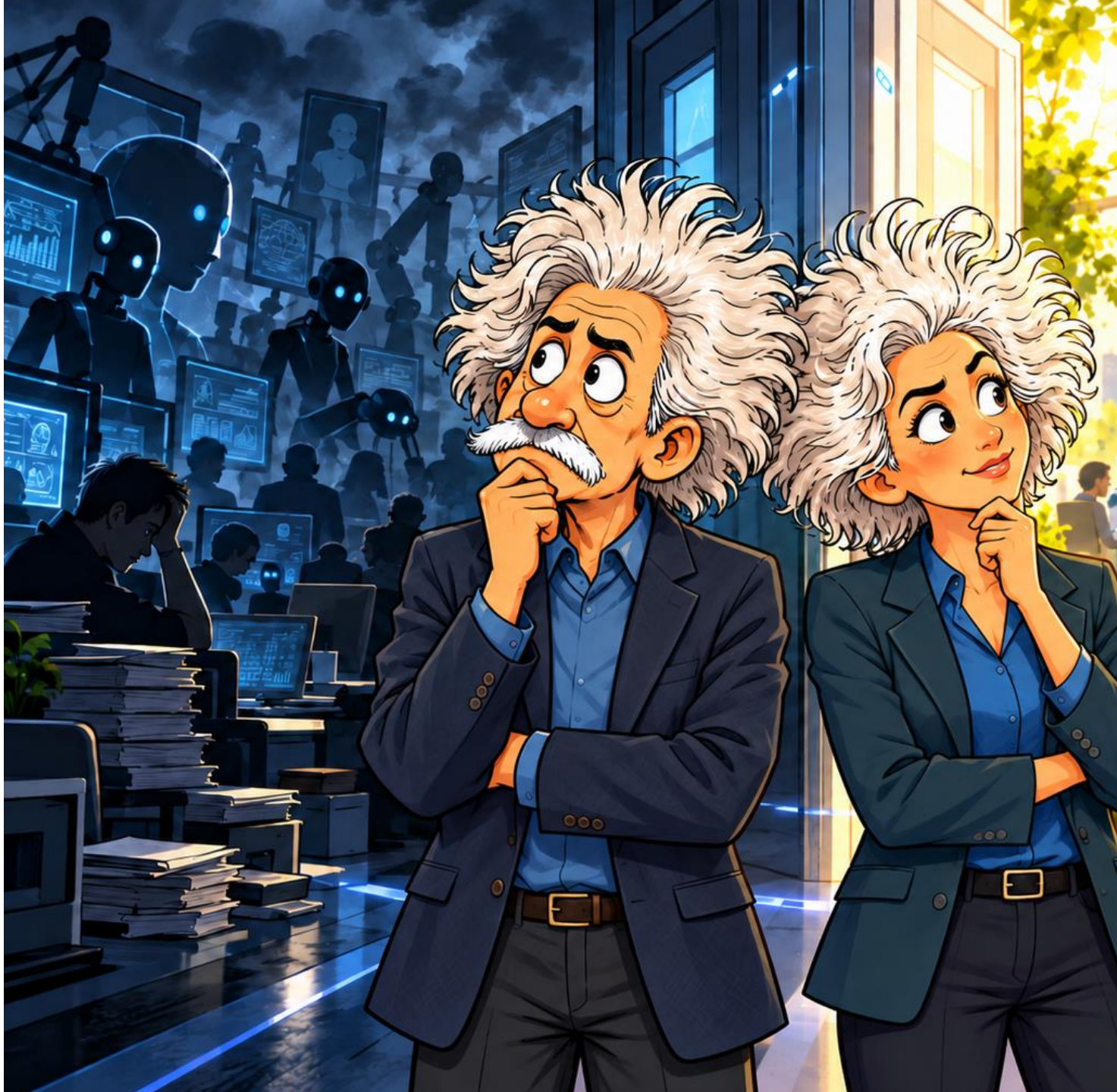


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Interactive group discussion – Q3

What are your personal feelings about AI in your professional role?

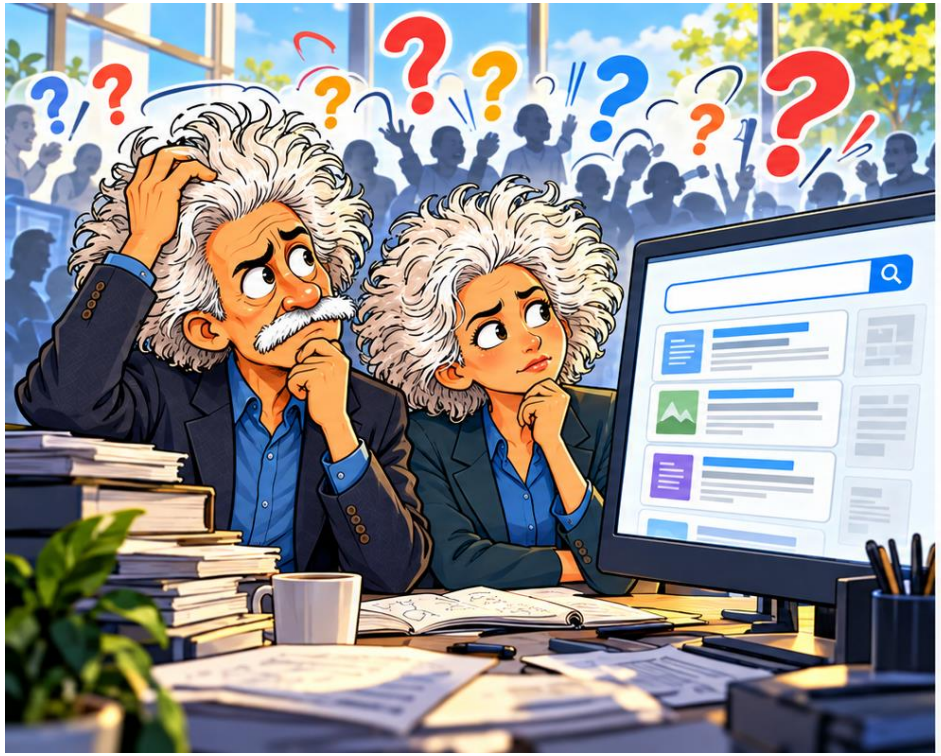
a) Worried
b) Looking forward to deeper implementation
c) Mixed feelings
d) No feelings



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Are we overreacting?

is AI just a more advanced Google and we will soon get used to it and will see it as a perfectly normal tool in the professional work?





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