MAKING SENSE OF COMPLEXITY: THE ROLE OF AI IN ADVANCING ONE HEALTH

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EUROPEAN FOOD SAFETY AUTHORITY

MAKING SENSE OF COMPLEXITY

NEW EUROPEAN COMMISSION

Olivér Várhelyi

Commissioner-designate for Health and Animal Welfare

You will also continue to build on the **One Health** approach, recognising the connection between people, animals, plants and their shared environment. You will be responsible for **animal welfare**. The last few years highlighted the importance of this approach and demonstrated the need for a true European Health Union.

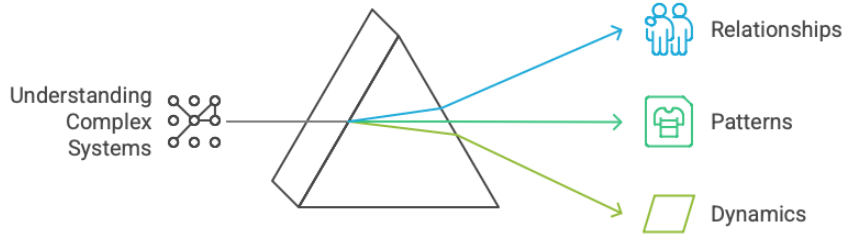
■ ■ ■

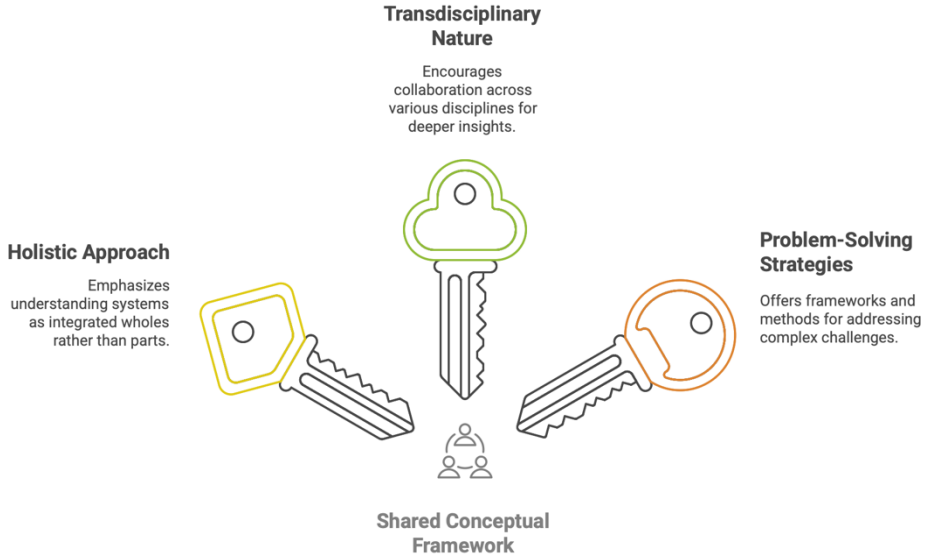
You should work to complete the **European Health Data Space**. You will promote the uptake of artificial intelligence, notably through clear and timely guidance on its use in the lifecycle of medicines. You will make proposals to **scale up genome sequencing capacities**.

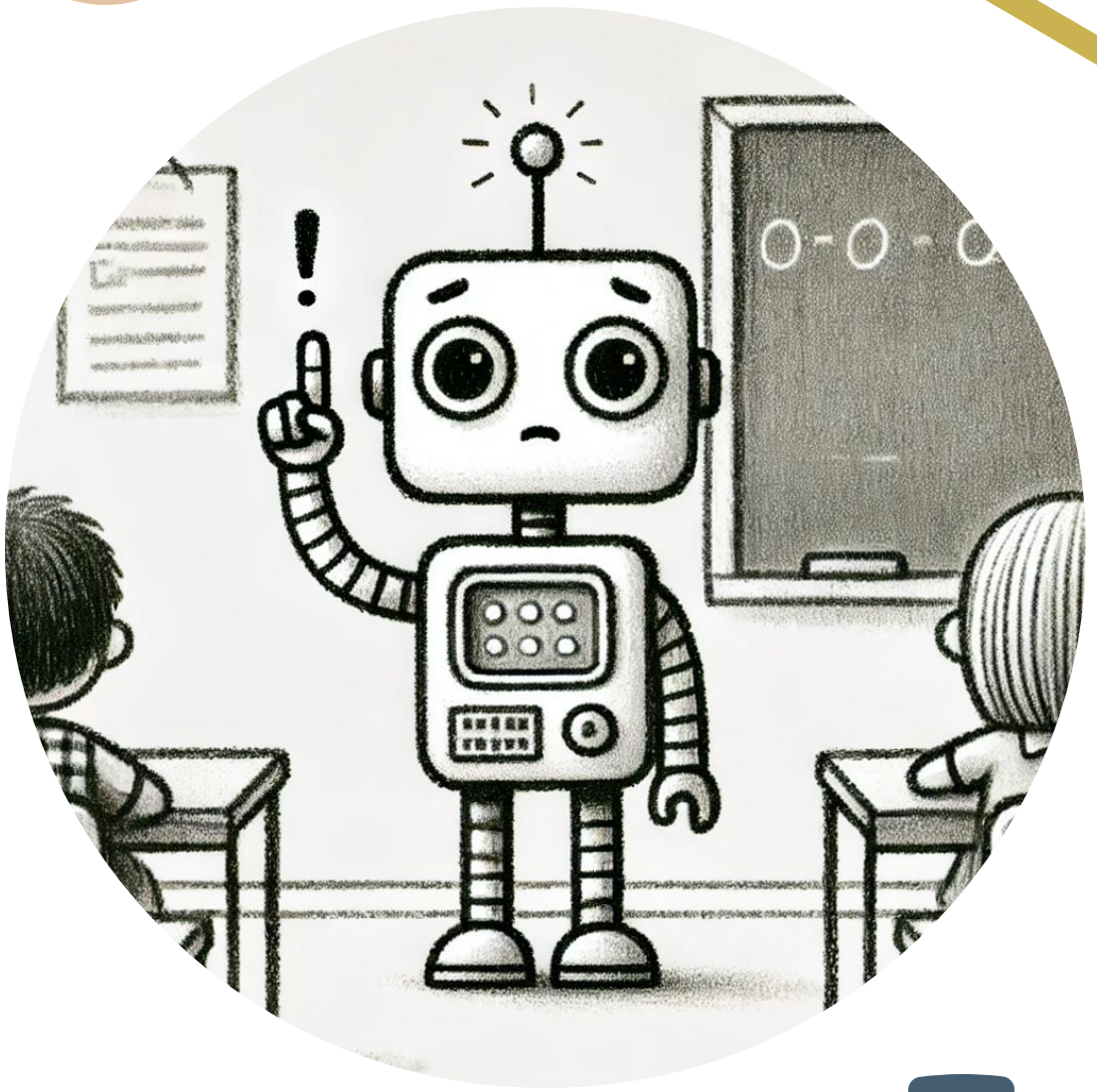
■ ■ ■

SYSTEMS APPROACH TO DEAL WITH COMPLEXITY IN OH

Systems thinking is a powerful approach for understanding and addressing complex problems across various domains.







AND ME?

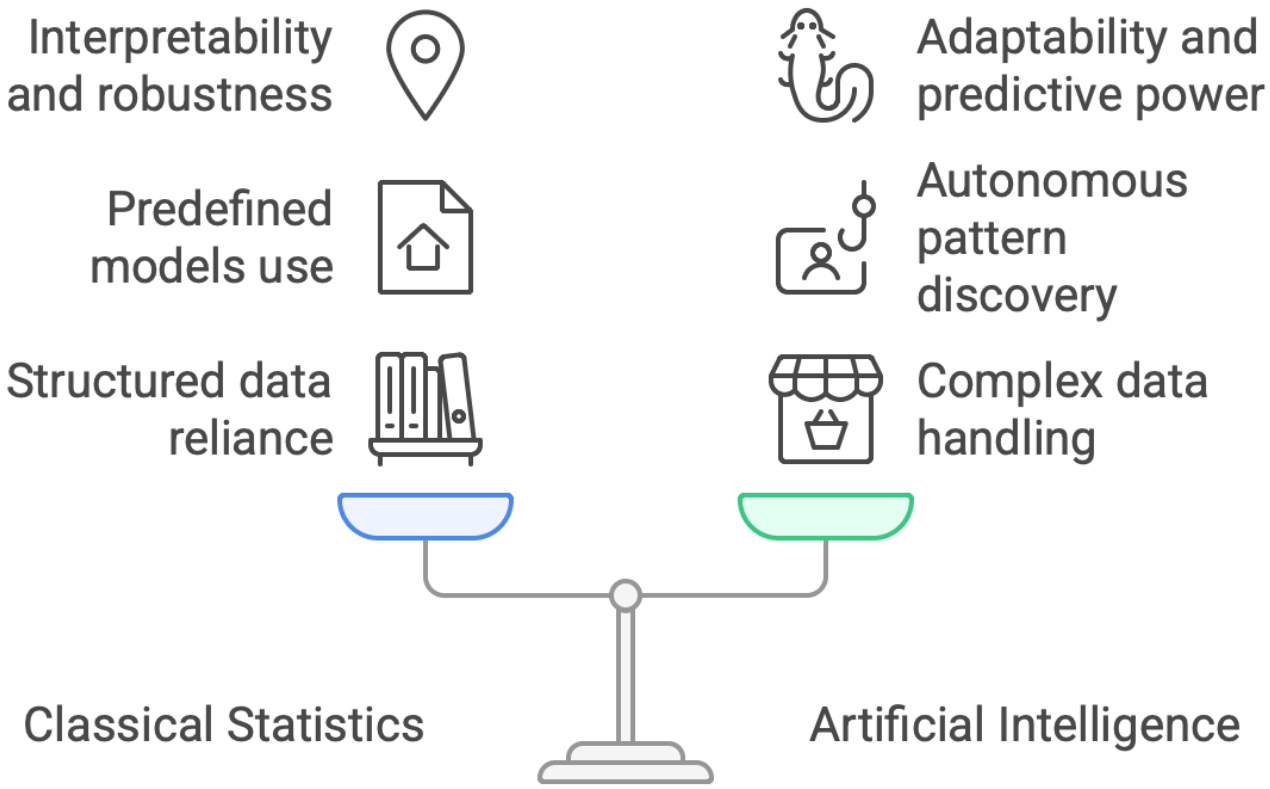
AI 101: THE BATH PROBLEM

How long does it take before my bath is empty?

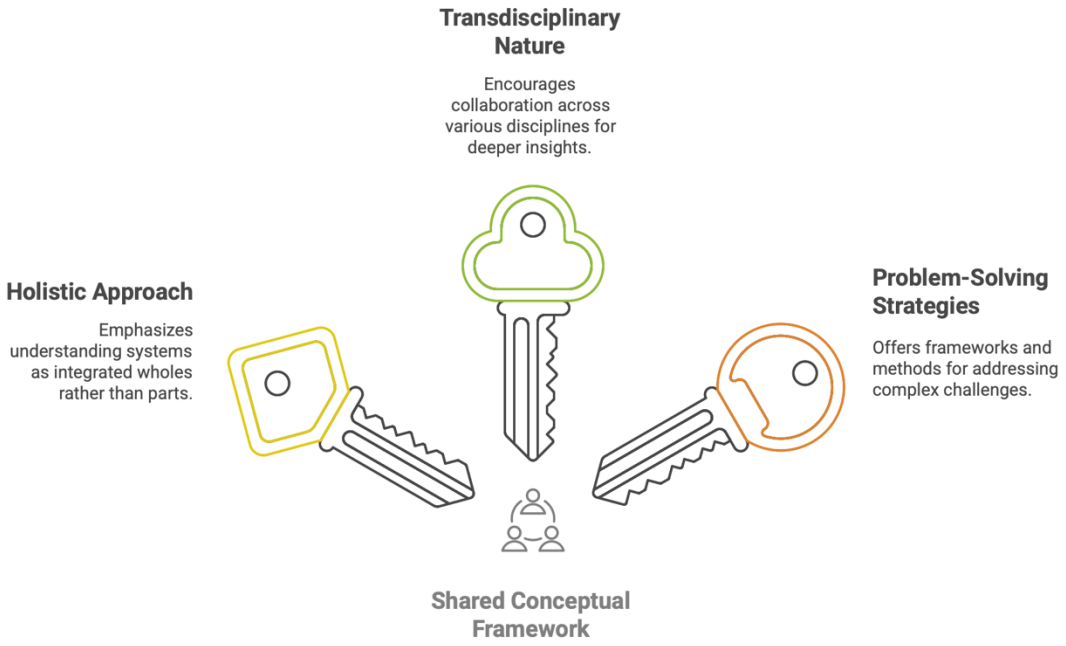
1 problem

different solutions depending on who sits in the bath

WHY AI


Interpretability and robustness
Predefined models use
Structured data reliance
Adaptability and predictive power
Autonomous pattern discovery
Complex data handling
Classical Statistics
Artificial Intelligence

AI IN ONE HEALTH



SOME SNIPPETS FROM LITERATURE

One Digital Health: A Unified Framework for Future Health Ecosystems

Arriel Benis [1 2], Oscar Tamburis [3], Catherine Chronaki [4], Anne Moen [5]

Affiliations + expand

PMID: 33492240 PMCID: PMC7886486 DOI: 10.2196/22189

Operationalizing "One Health" as "One Digital Health" Through a Global Framework That Emphasizes Fair and Equitable Sharing of Benefits From the Use of Artificial Intelligence and Related Digital Technologies

Calvin Wai-Loon Ho*

Review

Innovative applications of artificial intelligence in zoonotic disease management

Wenqiang Guo [a 1], Chenrui Lv [a 1], Meng Guo [b], Qiwei Zhao [a], Xinyi Yin [a], Li Zhang [a]

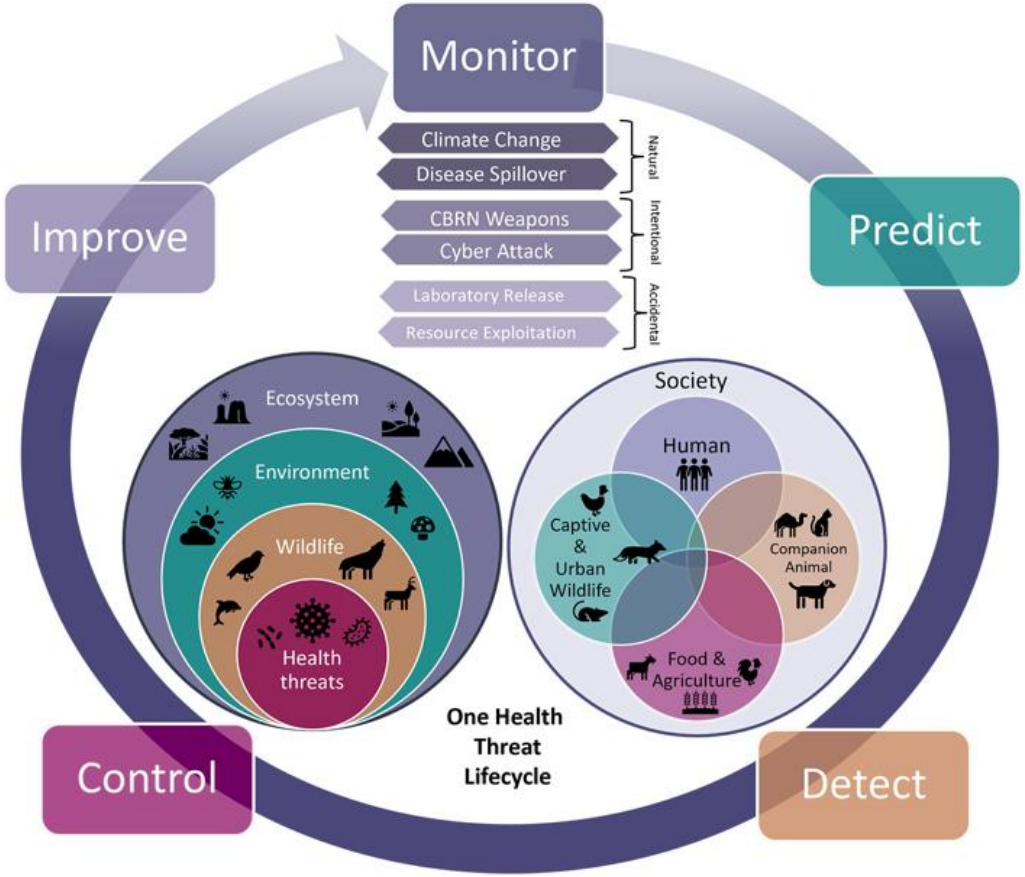
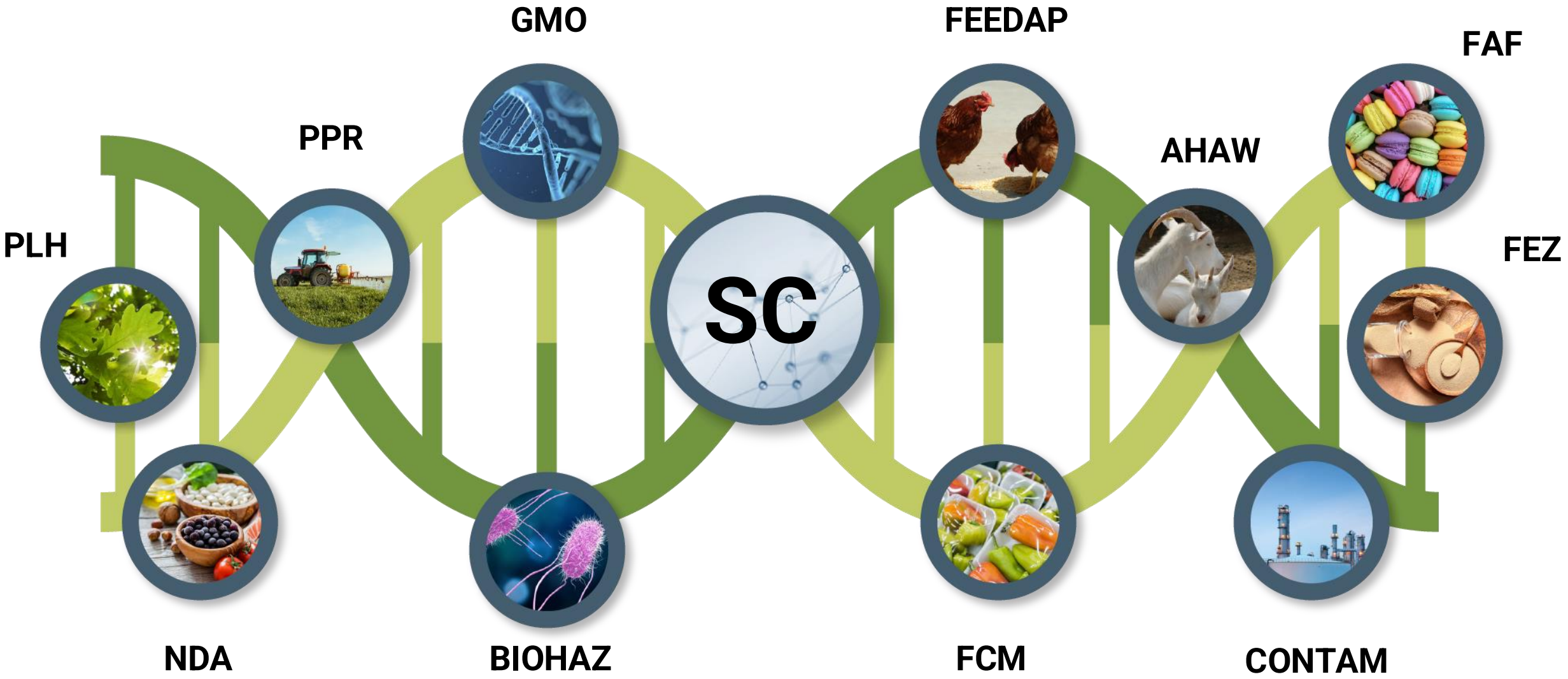


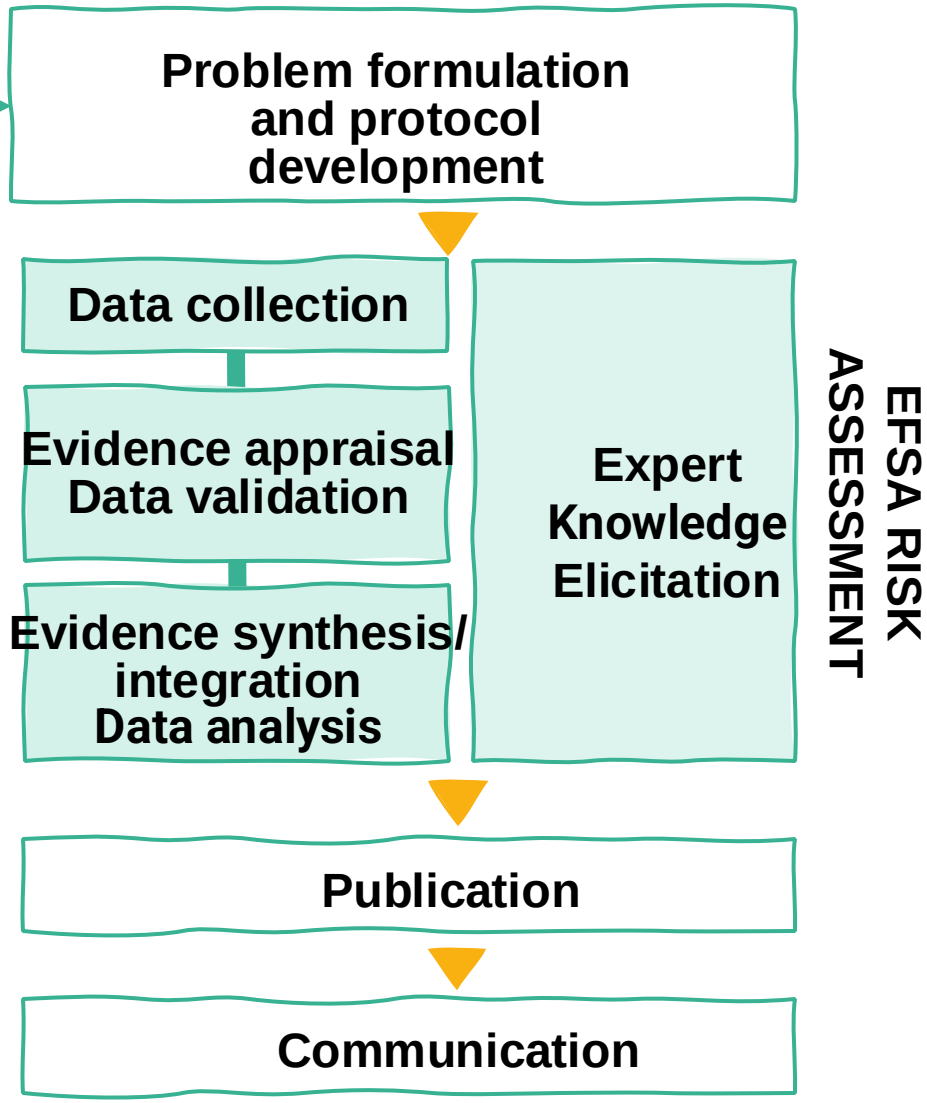
Illustration by Lauren Charles | Pacific Northwest National Laboratory


EFSA

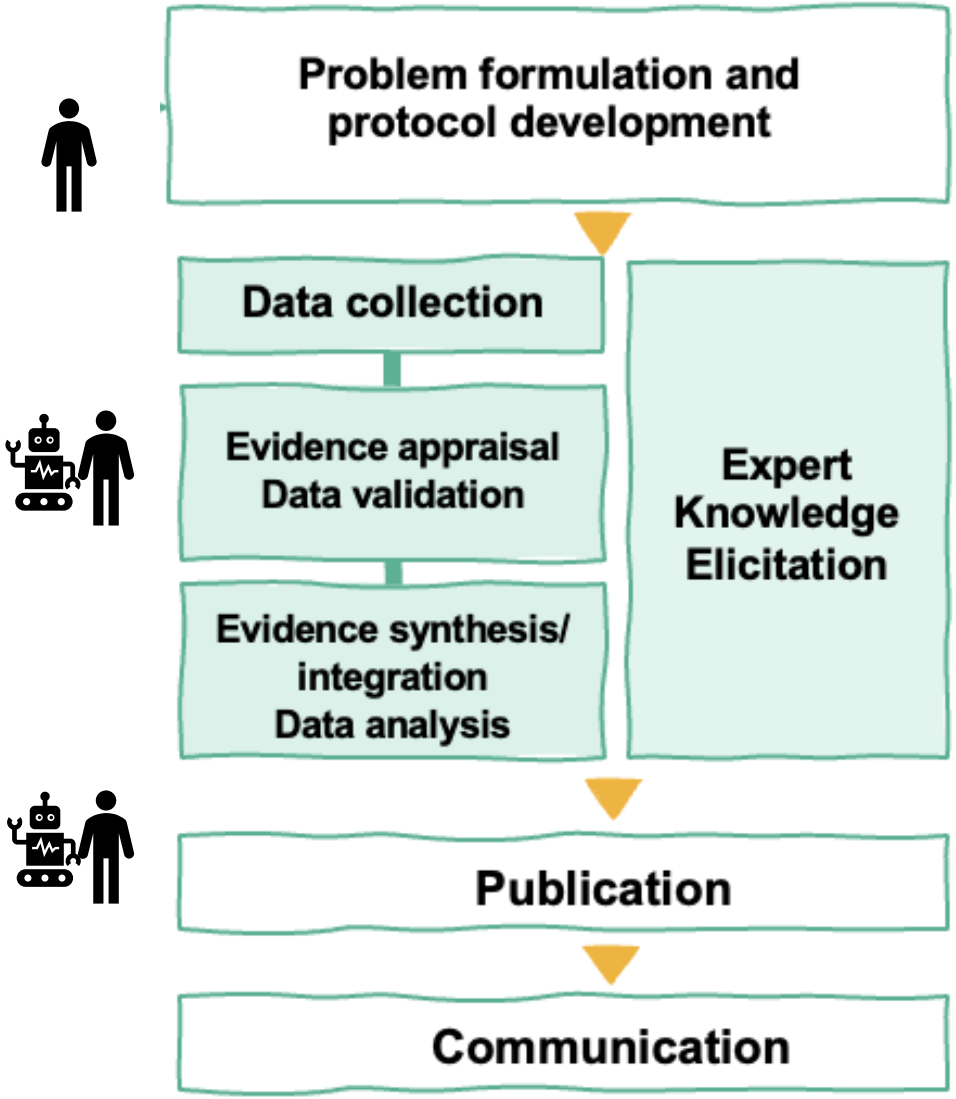
EFSA REMIT

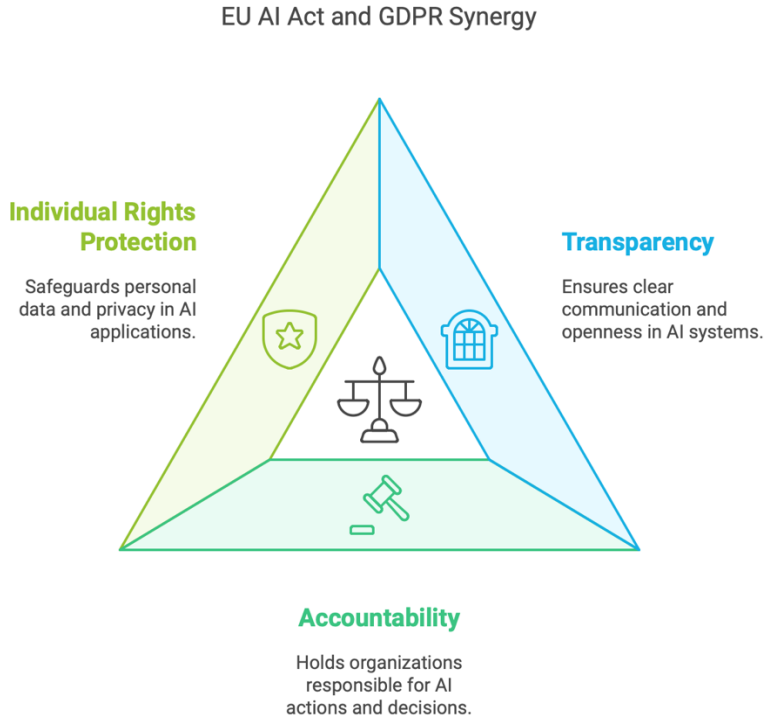


QUESTIONS AND ANSWERS

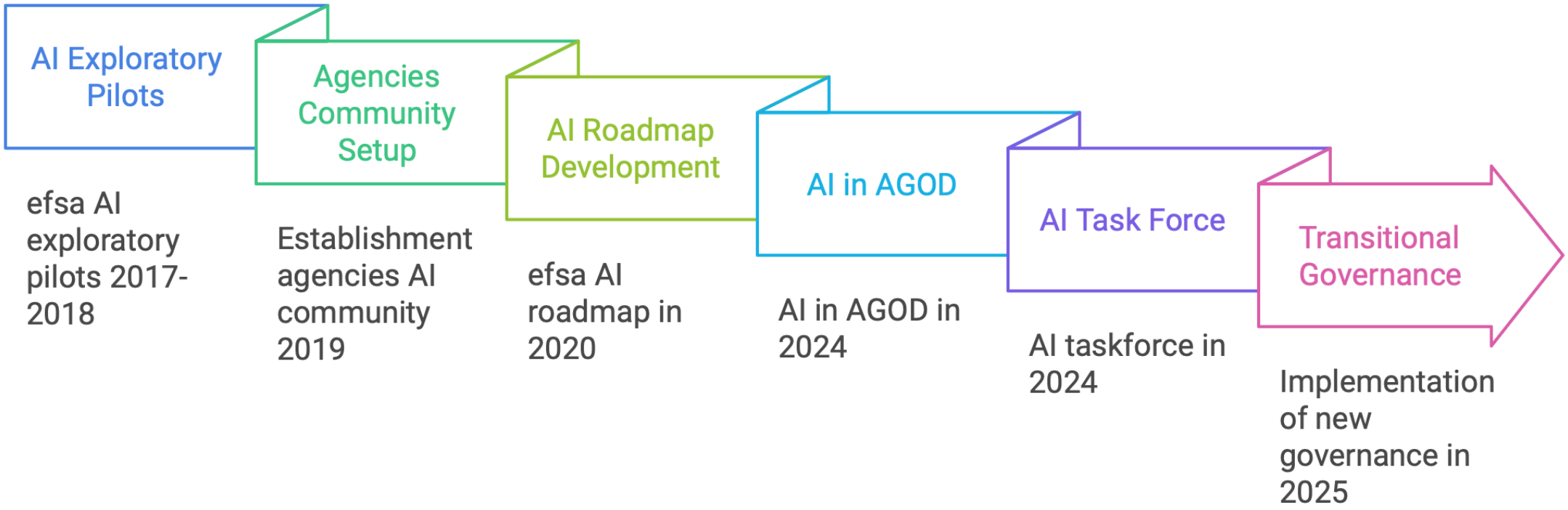


EFSA: EVIDENCE BASED RISK ASSESSMENT BACKBONE





AI JOURNEY IN EFSA



THE EFSA ROADMAP 2020

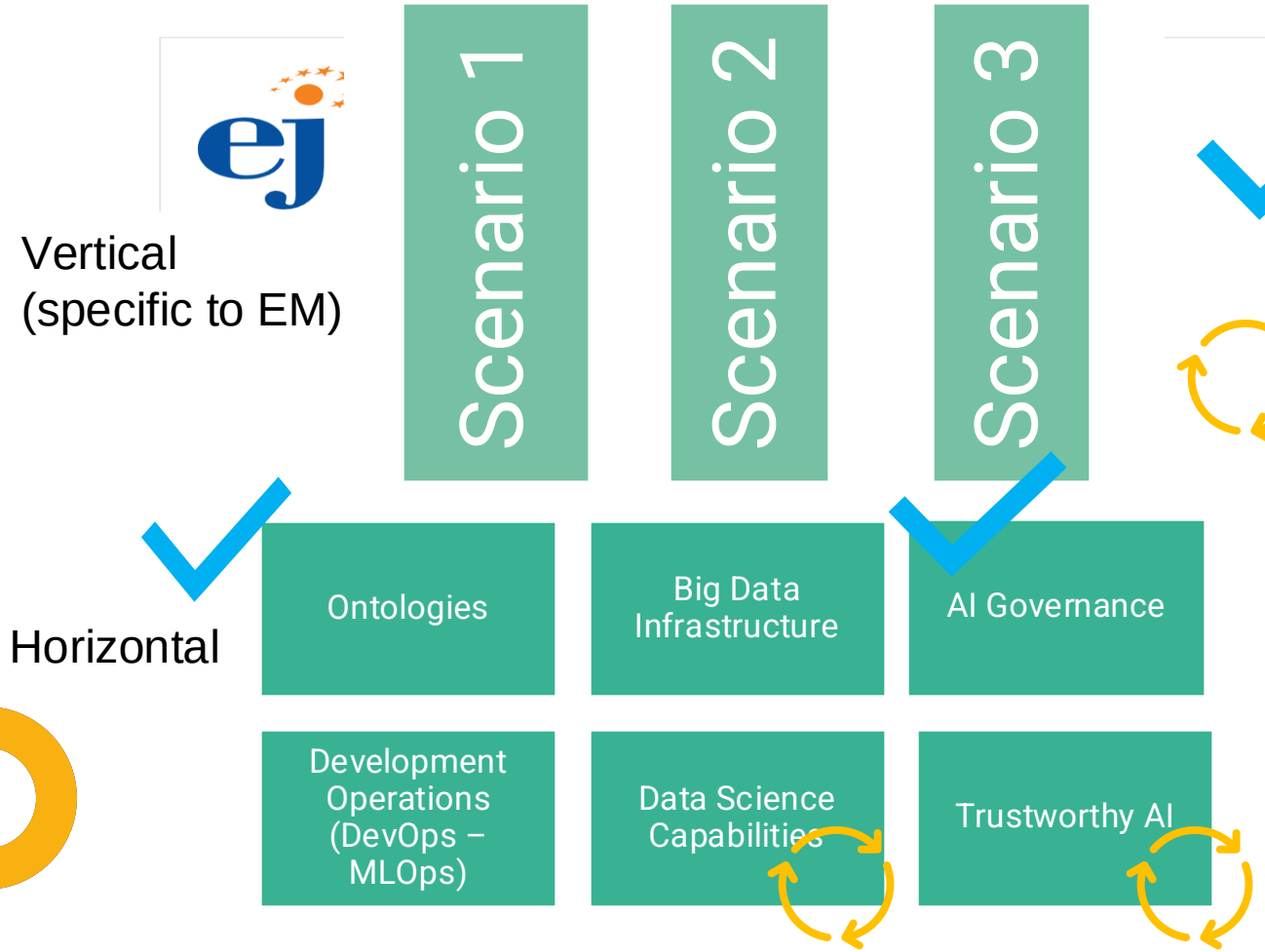
Artificial intelligence for evidence management in risk assessment

- **Vision:** by 2027 EFSA to achieve
  - i) an increase in the accessibility and the breadth of the body of evidence,
  - ii) enhancing the trustworthiness in the risk assessment process, and
  - iii) apply human centric artificial intelligence in close co-existence with the human expertise
- **Roadmap for action**: Oct 2021
- **Implementation**: Dec 2021 onwards

THE EFSA ROADMAP 2020-2027

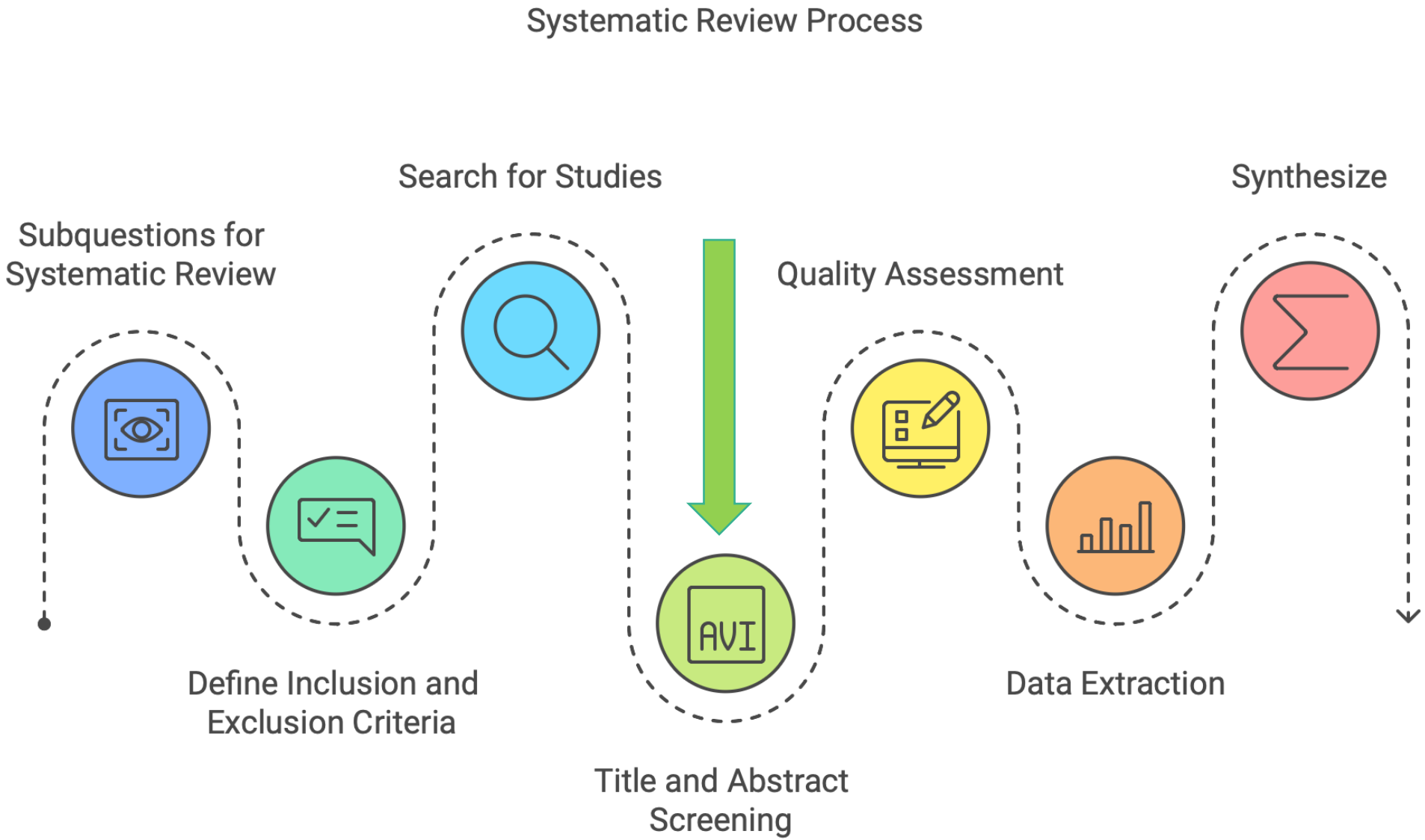
Roadmap for actions on artificial intelligence for evidence management in risk assessment

Published: 16 Maggio 2022 **Approved:** 1 Aprile 2022

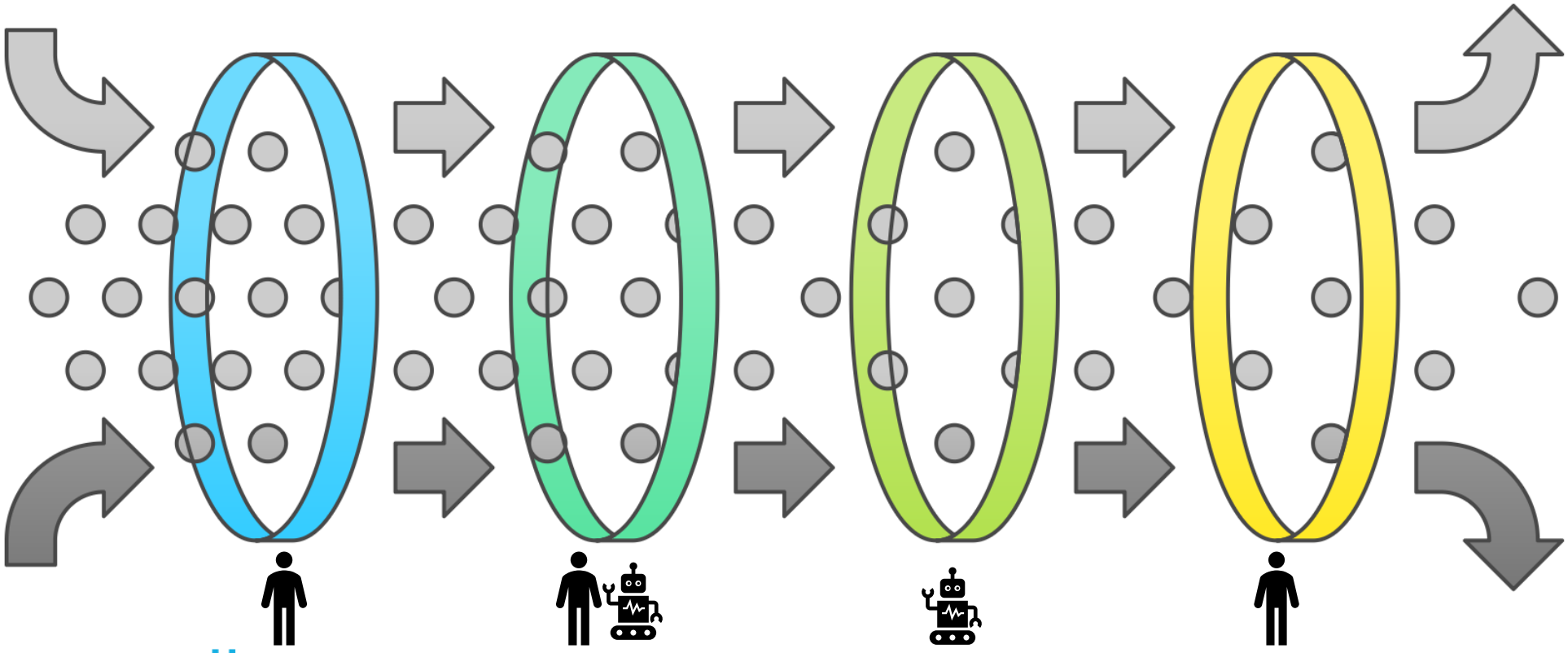


Use cases	Scenarios
Data Collection Terminology Assessment SLR Keywords Identification SLR Relevant Abstract Screening SLR Literature De-duplication Text Summarization SLR Literature Findings Clustering	1: buy
Quality Improvement of the Scientific Output	2: buy and adjust
Expert pool Identification Expert Selection Comparable Appraisals Detection	3: build by grant or procurement

ABSTRACT SCREENING



AI SUPPORTED ABSTRACT SCREENING



Human Screening

Inclusion and exclusion criteria.

AI Learning

AI learns and reorders results.

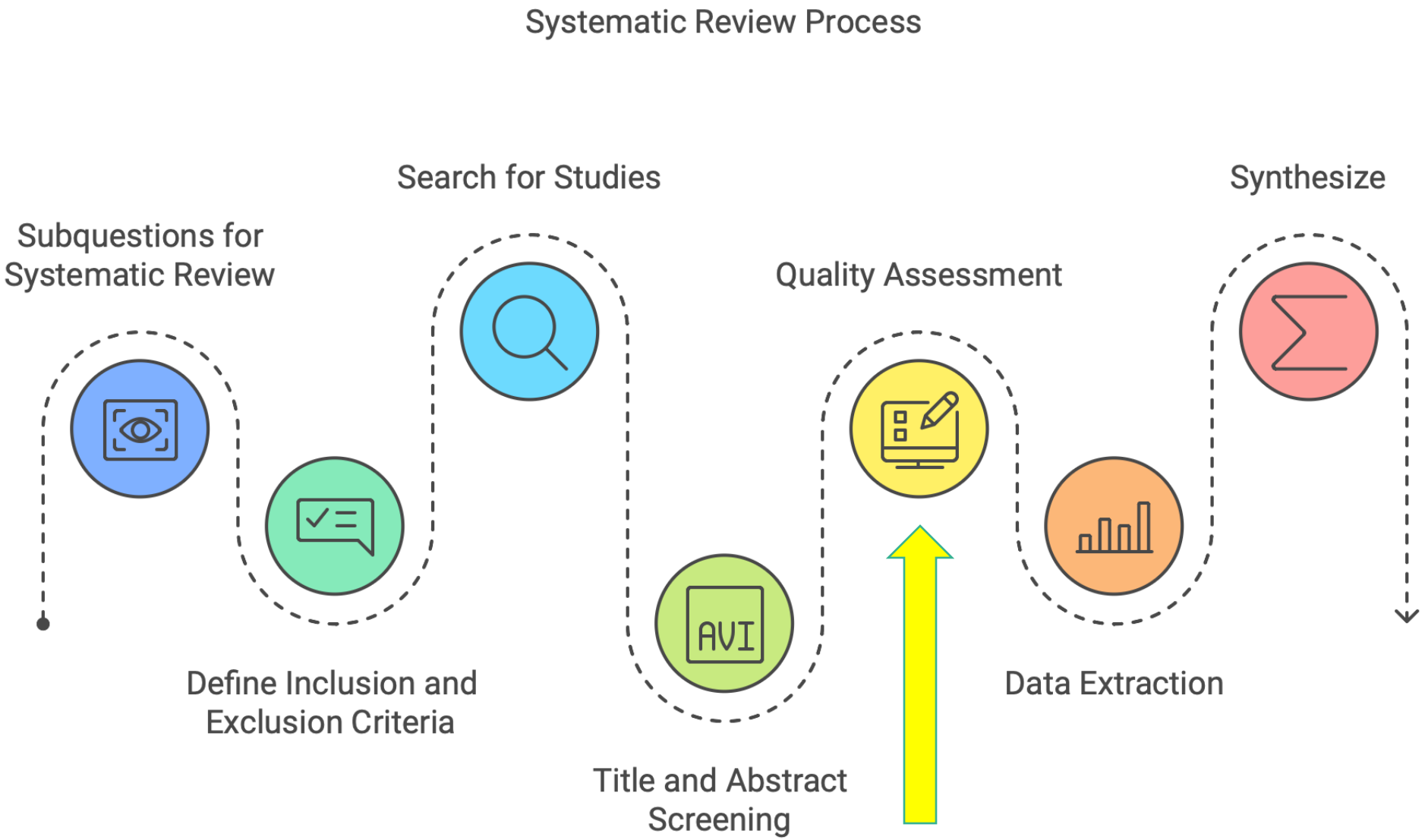
AI Screening

AI screens remaining results.

Human Review

Check final list

CRITICAL APPRAISAL



CRITICAL APPRAISAL WITH NTP OHAT - EXPERIMENTAL ANIMAL STUDIES

Q1 Was administered dose or exposure level adequately randomized?
Q2 Was allocation to study groups adequately concealed?
Q5 Were experimental conditions identical across study groups?
Q6 Were the research personnel and human subjects blinded to the study group during the study?
Q7 Were outcome data complete without attrition or exclusion from analysis?
Q8 Can we be confident in the exposure characterization?
Q9 Can we be confident in the outcome assessment?
Q10 Were all measured outcomes reported?
Q11a Were statistical methods appropriate?

HIGHLIGHTED PDF

Long-Term Toxicity and Carcinogenicity Study of Cyclamate in Nonhuman Primates

Highlighting colors legend

Main Question Code	Main Question Text
Q1	Was administered dose or exposure level adequately randomized?
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Q8	Can we be confident in the exposure characterization?
Q9	Can we be confident in the outcome assessment?
Q10	Were all measured outcomes reported?
Q11a	Were statistical methods appropriate?

the intestinal flora (Renwick, 1986). The ADI for cyclamate established by the JECFA (1982) and the SCF (1985) is based on the NOAEL for testicular atrophy produced by cyclohexylamine in rats with the application of a 100-fold safety factor and assuming 18% metabolism per day (see Renwick, 1986).

This report presents results of a toxicity and carcinogenicity study of cyclamate in nonhuman primates that involved treatment for a period of up to 24 years, i.e., from 1970 to 1994.

MATERIALS AND METHODS

Animals and dosing. Of the 21 monkeys used in this study, there were nine (seven males, two females) cynomolgus (*Macaca fascicularis*), nine (four males, five female) rhesus (*Macaca mulatta*), and three (two males, one female) African green (*Cercopithecus aethiops*) monkeys. These three species had been used in earlier chemical carcinogenesis studies in this monkey colony and had exhibited comparable sensitivity to different test compounds with respect to tumor incidence, latent period, and tumor type (Thorgeirsson *et al.*, 1994). They were born and raised in a closed colony. Infants were hand-reared and began receiving cyclamate (a gift from Abbott Laboratories, Chicago, IL) in the Similac formula within the first few days of birth. At 6 months of age, the monkeys were placed in individual, wall-mounted, stainless steel cages equipped with an automatic watering device. The daily diet consisted of *ad libitum* Purina High Protein Monkey Chow #5045, a vitamin sandwich, and half an apple. The sodium cyclamate (dissolved in warm water at 200 mg/ml) was incorporated into the vitamin mixture, which consisted of the following ingredients: powdered milk (5 pounds); Parvo (folic acid supplement, 4 oz., 20% with starch, Roche Agricultural Products); Cecon (vitamin C supplement, 300 ml, Abbott Laboratories, Chicago, IL); molasses (2 l); and water (500 ml). The appropriate amounts of the vitamin mixture containing sodium cyclamate (0.5 ml/animal for the 100 mg/kg group and 2.5 ml/animal for the 500 mg/kg group) were placed onto sandwiches. The monkeys (four cynomolgus, four rhesus, two African green) in the 100 mg/kg group received one sandwich daily 5 days per week. The monkeys (five cynomolgus, five rhesus, one African green) in the 500 mg/kg group received two sandwiches daily for 5 days per week. When the study was initiated in 1970, the rationale for selecting these doses was to provide an adequate safety margin in relation to human exposure. The 100 mg/kg and 500 mg/kg dose levels are about 9 and 45 times higher than the current upper limit of the ADI of 11 mg/kg/day established by the JECFA and SCF. A group of 16 control animals (eight cynomolgus, [five males and three females] and eight rhesus monkeys [six males and two females]) received the vitamin sandwiches without sodium cyclamate. The monkeys were evaluated daily and weighed once a week. Physical examination was carried out by a veterinarian every 6 months when blood was drawn for

poor replicate values (>5% difference) were subject to further analyses to confirm the results. Triplicate standard curves of 3–5 different concentrations of cyclohexylamine spiked into the biologic matrix from control animals were analyzed with the samples; these were linear over the ranges studied (0–2 μg/ml for plasma; 0–10 μg/ml for urine; 0–10 μg/ml homogenate for testes) and showed intra-assay variability of 7% or less at each concentration. The sample data represent the means of 2–4 replicate values mostly within ±5%.

The urine samples showed a very wide range of concentrations of cyclohexylamine, so that they had to be diluted to different extents—up to 1 in 100. In each case, 0.5 ml of the final dilution was used for analysis. The testicular samples were homogenized in 0.1 M phosphate buffer, and aliquots were extracted and analyzed. Samples from control monkeys showed a small interfering peak on HPLC that corresponded to low concentrations of cyclohexylamine (see Results).

RESULTS

This study included 21 cyclamate monkeys and 16 age-matched controls (see Tables 1–3). The monkeys were dosed from a few days after birth until the time of death. In 1994 when a decision was made to terminate the study, 7 cyclamate-treated monkeys had died and 14 were still alive. A cyclamate-treated monkey (789J; 500 mg/kg dose) died accidentally at 2 years of age and did not show any specific abnormalities when necropsied. A second monkey (790J; 500 mg/kg dose) died at 7 years of age and showed renal tubular degeneration. No other problems were documented until 1985, when two monkeys (769J; 100 mg/kg, and 800J; 500 mg/kg) died during a varicella outbreak. The same year, one monkey died as a result of chronic myocarditis (782J; 500 mg/kg) and two females were euthanized due to severe symptoms from extensive pelvic endometriosis (773J; 100 mg/kg, and 795J; 500 mg/kg). When the cyclamate study was terminated in 1994, the remaining eight monkeys in the 100 mg/kg group and six in the 500 mg/kg group, as well as the controls, were euthanized and necropsied. At that time, kyphosis was observed in three of the cyclamate monkeys. No other external abnormalities or health problems were noted. Results of blood samples collected from these animals did not reveal any abnormalities in blood cell counts, liver function tests, electrolytes, or BUN (results not shown).

SUMMARY DOCUMENT

AutoCAT Summary

Q1	Was administered dose or exposure level adequately randomized?

introduction

This report presents results of a toxicity and carcinogenicity study of cyclamate in nonhuman primates that involved treatment for a period up to 24 years, i.e., from 1970 to 1994.

In 1970, a report by an increased incidence of bladder tumors in rats dosed with a mixture of sodium cyclamate and sodium saccharin led a ban on the use of cyclamate as an artificial sweetener in a number of countries, including the United Kingdom and the United States.

MATERIALS AND METHODS

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Evaluation of testicular function was carried out in 1982, after 12 years of dosing, in twelve cyclamate-treated monkeys (numbers 786J, 7 771J, 774J, 782J, 784J, 785J, 786J, 787J, 799J, 800J, 943M) and the age-matched controls.

When the study was terminated in 1994, the surviving cyclamate-treated monkeys included ten males. With one exception (see below, monkey number 771J), the testicular size, color, and consistency of the cyclamate groups were not different from that of the age-matched controls.

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YES/NO