Critical Analysis of the Consensus Key Characteristics Approach Case Study on Carcinogens and Endocrine Disruptors

Bottom-Line Up-Front

The Consensus Key Characteristics Approach (CKCA) applied to carcinogens or endocrine disruptors is either: **1. Unscientific:** as it cannot be falsified (all endogenous and biologically relevant chemicals are carcinogens and endocrine disruptors); or **2. False:** CKCA rewards confirmation bias. Evidence of meeting 1 single criterion is sufficient to be labeled a Carcinogen or Endocrine Disruptor. Proponents specifically state the following question should be answered: "Does exposure to the agent induce end points associated with one or more specific key characteristic properties of carcinogens?"

Criteria for Scientific vs Unscientific

Criterion 1: Science is based on deductive logic

<u>Criterion 2</u>: Theories must be falsifiable

<u>Criterion 3</u>: The Scientific Enterprise advances by trying to disprove theories, through severe testing, rather than to affirm them

<u>Corollary</u>: Theories that are made or modified to be compatible with all observations about a subject are not scientific because they cannot be falsified

The Problem With Induction

Inductive reasoning requires circular reasoning. All observed instances of A have been B. Therefore, the next instance of A shall be B.

This logic requires the Uniformity Principle that all things true for the training set (past) are true for future inferences.

Circular logic: Future instance of A shall be B because past instances of A shall be B. Past instances of A shall be B because the future instances of A shall be B.

Fallacy: hasty generalization/stereotyping

CKCA Is Based On Induction

All observed instances of cancer causing/EDC chemicals have at least 1 key characteristic. Therefore, the next cancer causing/EDC chemical shall exhibit at least 1 key characteristic.

Thus exhibiting at least 1 key characteristic of cancer or endocrine disruption is both necessary and sufficient.

Lyle D. Burgoon, Ph.D., Fellow ATS¹ and Christopher J. Borgert, Ph.D.^{2,3} ¹Raptor Pharm & Tox, Ltd, New Hill, NC; ²University of Florida Dept. of Physiological Sciences, College of Veterinary Medicine, Gainesville, FL, and ³Applied Pharmacology and Toxicology, Inc, Gainesville, FL

CKCA Is Illogical by Deduction

Similar to the all swans are white conjecture. Evidence of a single black swan is sufficient to demonstrate the argument is illogical.

All observed instances of cancer causing/EDC chemicals have at least 1 key characteristic. Therefore, the next cancer causing/EDC chemical shall exhibit at least 1 key characteristic.

Thus, evidence of a single chemical that violates the theory is sufficient to deem the statement illogical.

CKCA Built on Confirmation Bias

It appears that the CKCA authors did not attempt to severely test and disprove their theories.

Severe testing requires one to attempt to disprove postulated theories. CKCA authors did not provide evidence that they considered chemical counter examples that would disprove the Key Characteristics identified

Case Study: Linoleic Acid (LA)

We searched PubMed using CKCA for Carcinogens "induces oxidative stress" and CKCA for Endocrine Disruptors "interacts with a hormone receptor" along with Linoleic Acid and found reports for both terms.

However, LA induces apoptosis in breast cancer cells, may be protective against certain cancers; no evidence of adverse endocrine action

Chemical	CKCA Carcinogens	CKCA Endocrine Disruption
Water	Alters Cell Proliferation, Cell Death, or Nutrient Supply	Alters the Fate of Hormone-Producing or Hormone-Responsive Cells
Adenosine Triphosphate	Alters Cell Proliferation, Cell Death, or Nutrient Supply	Alters Signal Transduction in Hormone-Responsive Cells
Calcium	Modulates Receptor- Mediated Effects	Alters Signal Transduction in Hormone-Responsive Cells
Sodium	Modulates Receptor- Mediated Effects	Alters Signal Transduction in Hormone-Responsive Cells
Glutathione	Alters Cell Proliferation, Cell Death, or Nutrient Supply	Alters Signal Transduction in Hormone-Responsive Cells

CKCA is Unreliable for Risk Assessment

Using Karl Popper's criteria, we have demonstrated that:

- CKCA is circular reasoning
- CKCA is illogical
- knowledge

Therefore, CKCA is unreliable for use in hazard and risk assessment

For More Information:

Lyle D. Burgoon <u>burgoon.lyle@raptorpharmtox.com</u>

Chris J. Borgert <u>cjborgert@apt-pharmatox.com</u>

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CKCA does not hold true and is inconsistent with current scientific

