U.S. FOOD & DRUG ADMINISTRATION

Science and Generic Drugs

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Definition

Science, noun:

1. A branch of knowledge or study dealing with a body of facts or truths systematically arranged and showing the operation of general laws.
2. Systematic knowledge of the physical or material world gained through observations and experimentation
3. A disciplined questioning of observations

Scientific Method

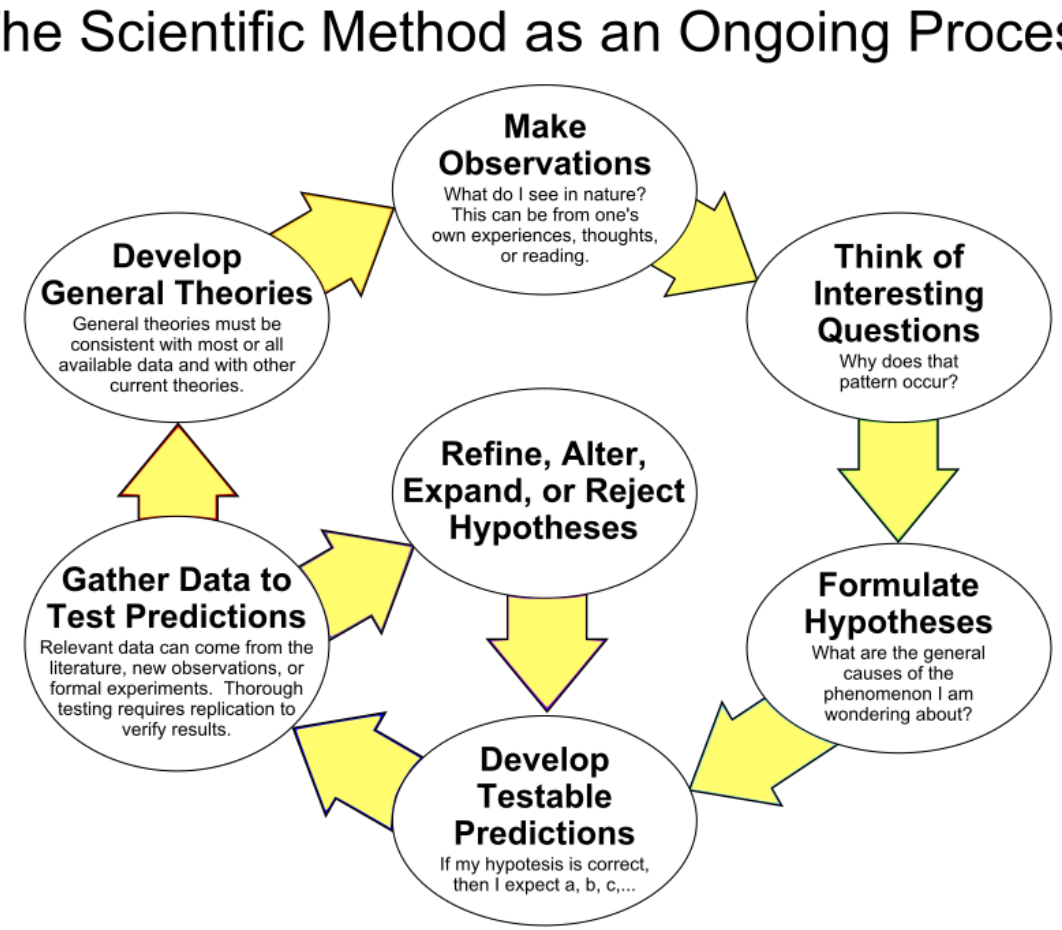
A method of research in which a problem is identified, relevant data are gathered, a hypothesis is formulated, and the hypothesis is empirically tested.

Scientists question “authorities” and “facts”

Scientists always ask “Why”

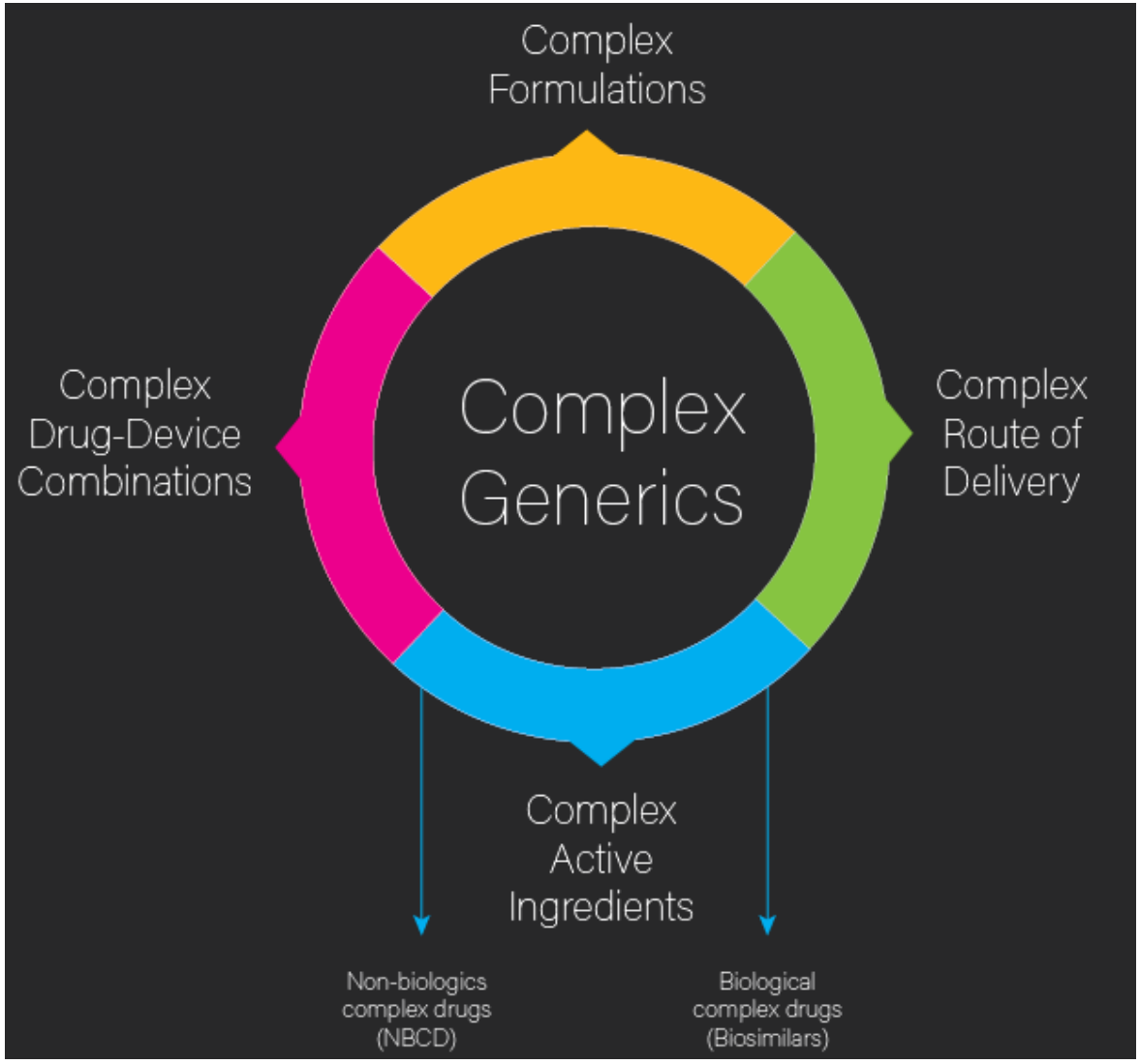
Science is an iterative process of observation, hypothesis generation, and testing of the hypothesis

“Why?” Never Goes Away



Theodore Garland, “The Scientific Method as an Ongoing Process”, 2015, University of California

Complex Drugs



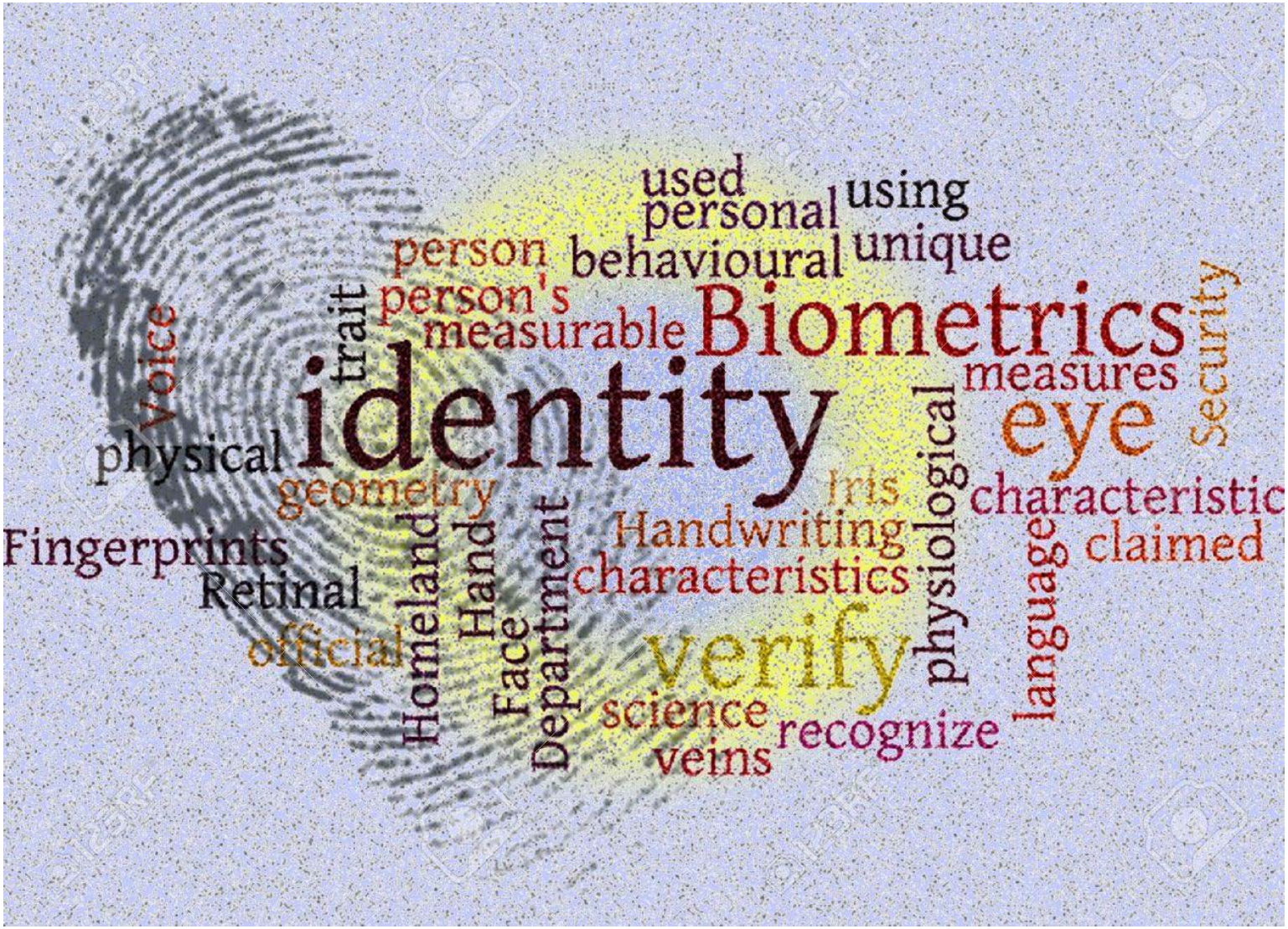
Innovator vs Generic

For an innovator drug product the criteria for approval are demonstration of Efficacy and Safety

For a generic drug approval the criterion is demonstration of a “shared identity” with the reference product. Shared identity means Efficacy and Safety can be inferred.

Generic drug approval is really a forensic process.

Identity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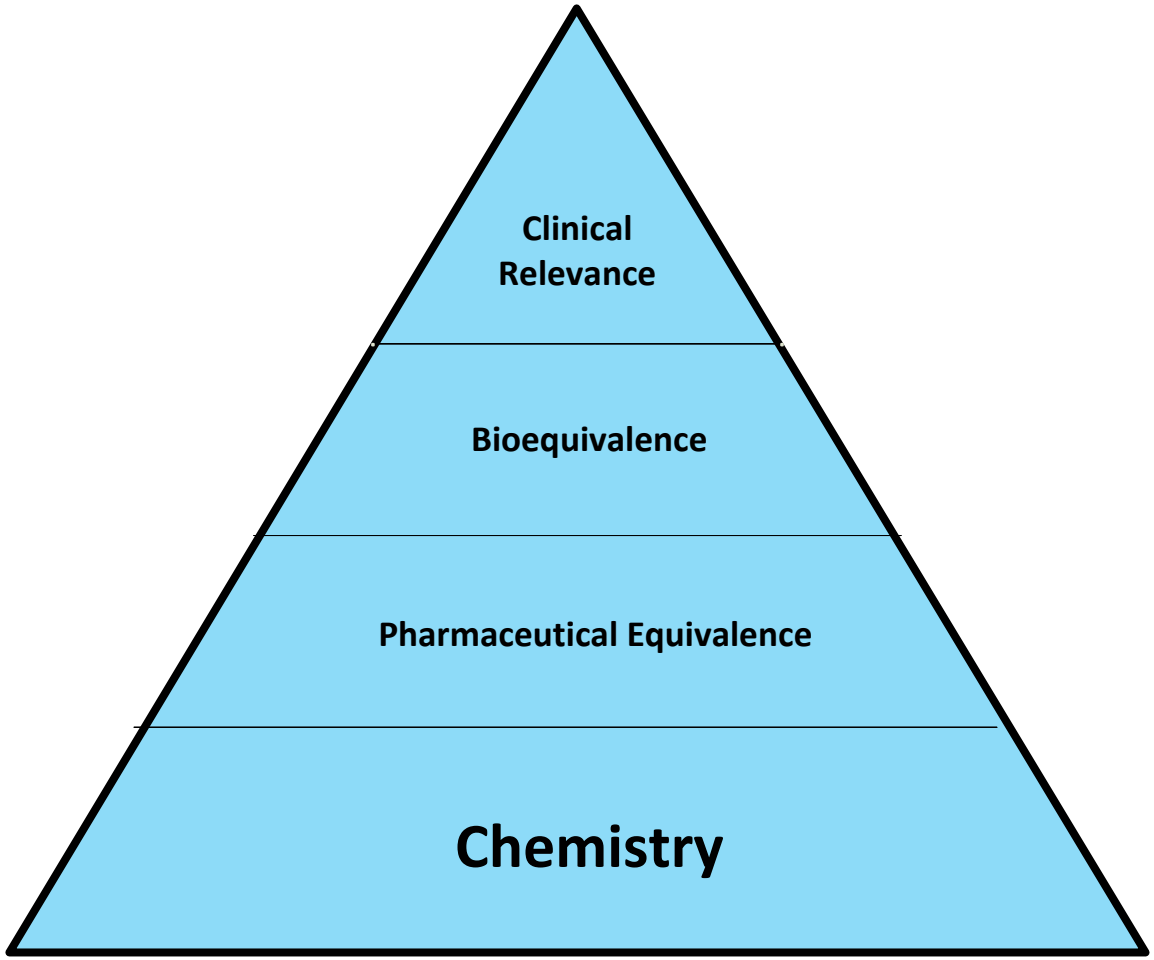
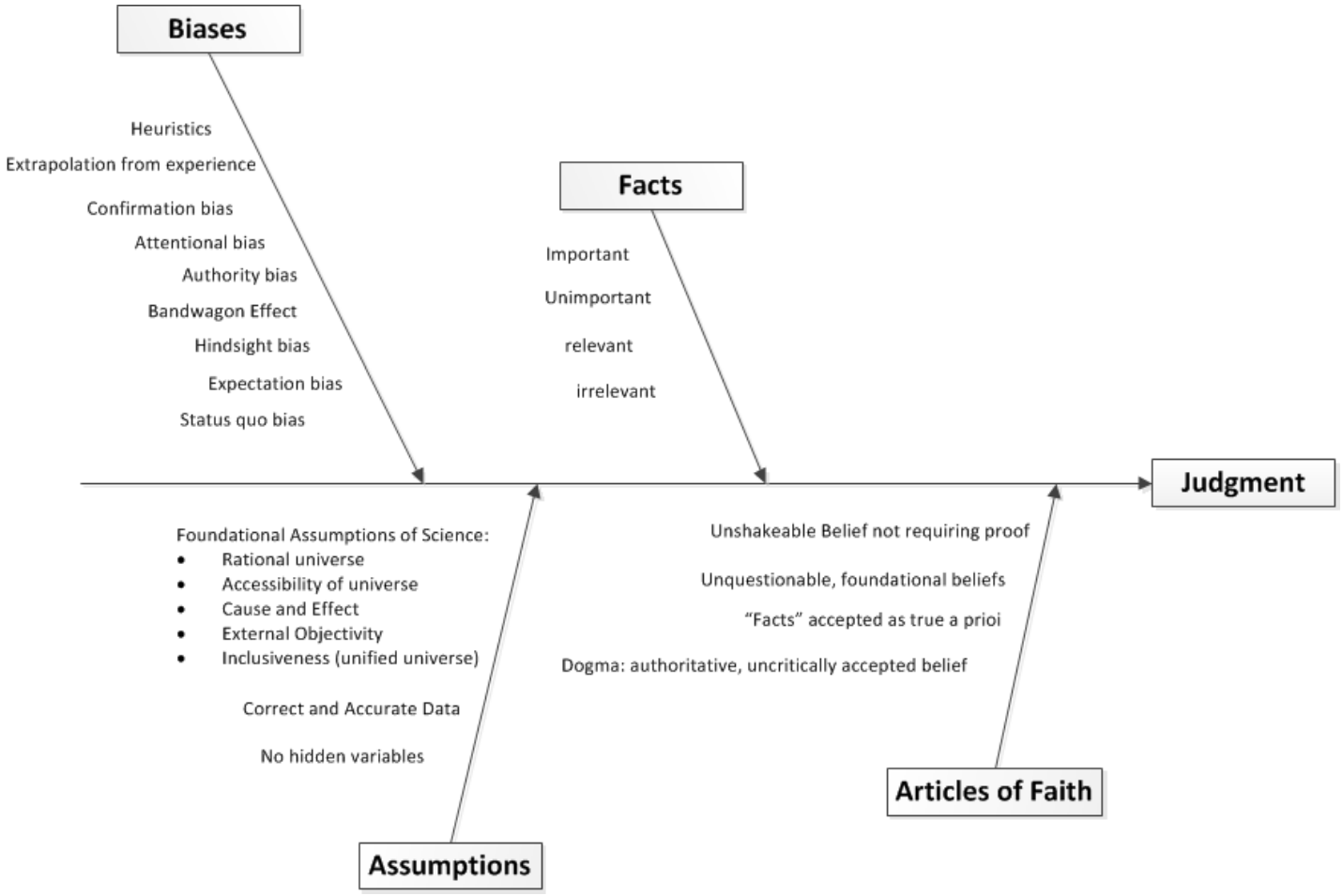
Identity of Generic Drugs



Equivalence is a Judgment not a Fact



Critical Elements of Identity

No Significant Differences from the RLD

- ***CHEMISTRY:*** The physiological effects of the active pharmaceutical ingredient (API) is the basis for development of the drug
- ***PHARMACEUTICAL EQUIVALENCE:*** the foundation of generic equivalence is a formulation developed as a means of delivering the API
  - Same active ingredient(s)
  - Same strength
  - Same dosage form
  - Same route of administration
- ***Bioequivalence:*** supports true pharmaceutical equivalence
  - absence of a significant difference in the **rate** and **extent** of absorption after administration
  - **available at the site of drug action** when administrated at the same molar dose under similar conditions
- ***Clinical Relevance:*** supports therapeutic equivalence in the context of the intended target population and for the same duration of therapy

Critical Review Elements for Generics

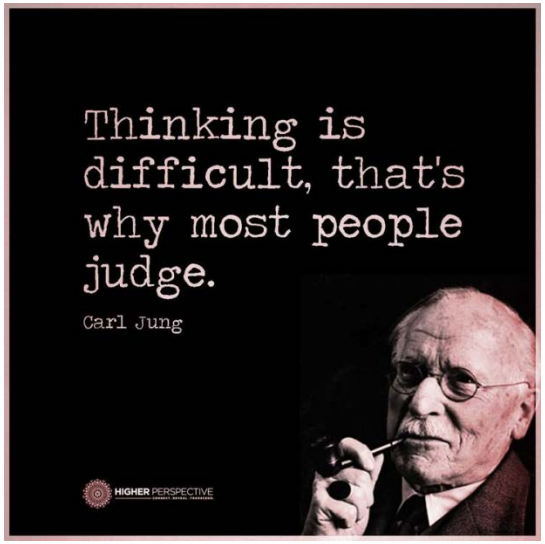
- **Chemistry**
  - Drug Product
  - Dose Form
  - Specifications
  - Impurities
  - Formulation
- **Bioequivalence**
  - Pharmacokinetics
  - Pharmacodynamics
  - In vitro Characterization
  - Statistics
  - Formulation
  - Impurities
  - Clinical Intent of Product Design
    - Clinical Use
    - Target Populations
    - Specific Indications
    - Chronicity of Use
- **Inspections**
  - Facility
  - Bioanalytic
  - Clinical
- **Labeling**
- **Legal/Regulatory**
  - Federal Food, Drug, and Cosmetics Act
  - Hatch-Waxman Amendment
  - Code of Federal Regulations
  - FDAAA
  - FDASIA
  - Precedent
  - Citizen Petitions

Why?

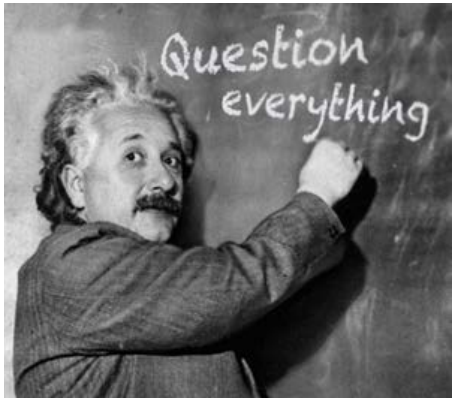
A technician will use the tools of science to measure and collect data for analysis.
Data collected and analyzed will be based on the defined critical elements of identity.

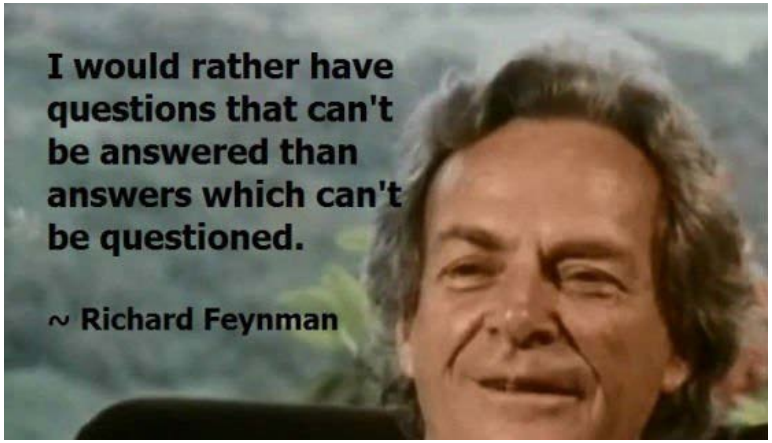
A scientist will ask "Why" and "What"?
Why are these elements important?
What are my possible biases, beliefs, and articles of faith that lead me to label these elements as critical?
Why are these and no others used to define "significant difference"?

Questions?


Thinking is difficult, that's why most people judge.
Carl Jung
HIGHER PERSPECTIVE


YOU ARE WHAT YOU REPEATEDLY DO. EXCELLENCE IS NOT AN EVENT, IT IS A HABIT.
Lifehack


Question everything


I would rather have questions that can't be answered than answers which can't be questioned.
~ Richard Feynman