Principles of GLP – EPA vs OECD

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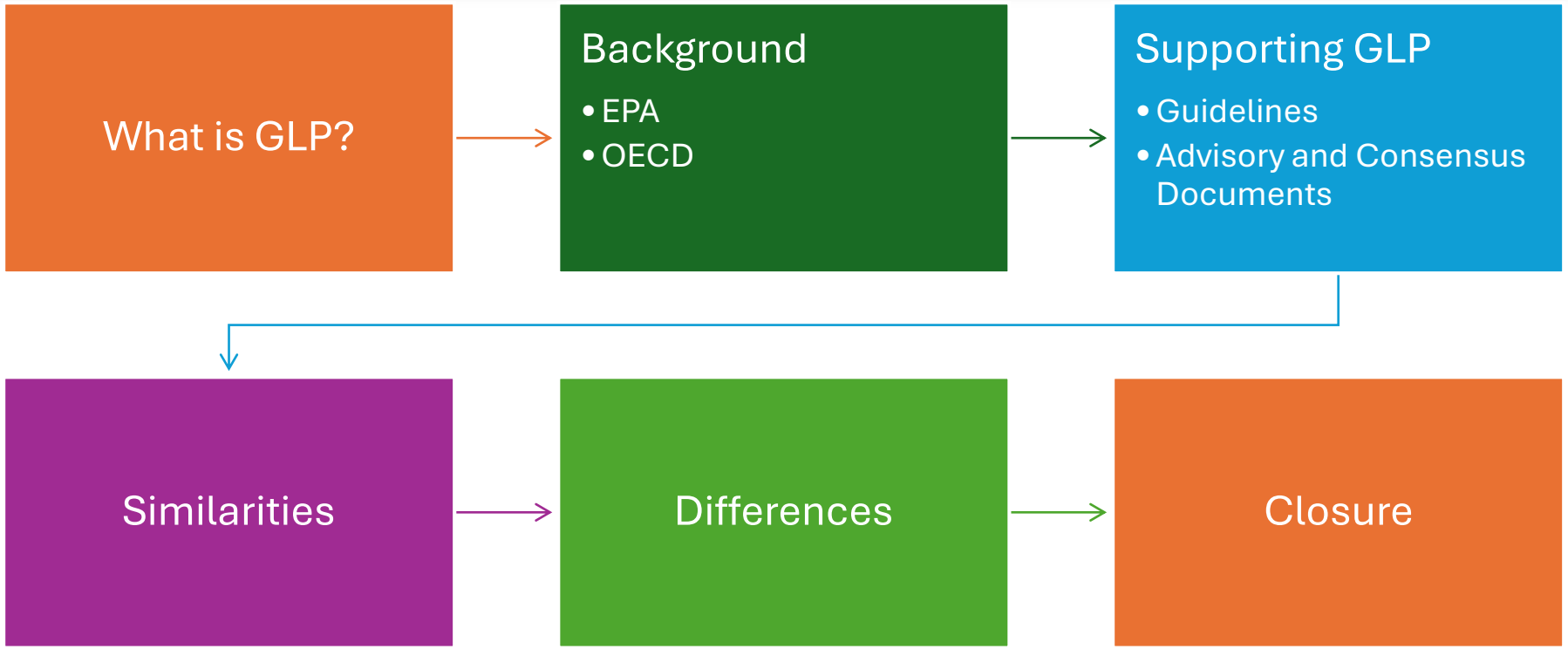
Agenda


What is GLP?
Background
• EPA
• OECD
Supporting GLP
• Guidelines
• Advisory and Consensus Documents
Similarities
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Closure

What is GLP?

Set of principles designed to guarantee the quality of nonclinical laboratory studies that support or are intended to support applications for research or marketing permits.

A quality management system not scientific management

Ham and Bananas Hollandaise

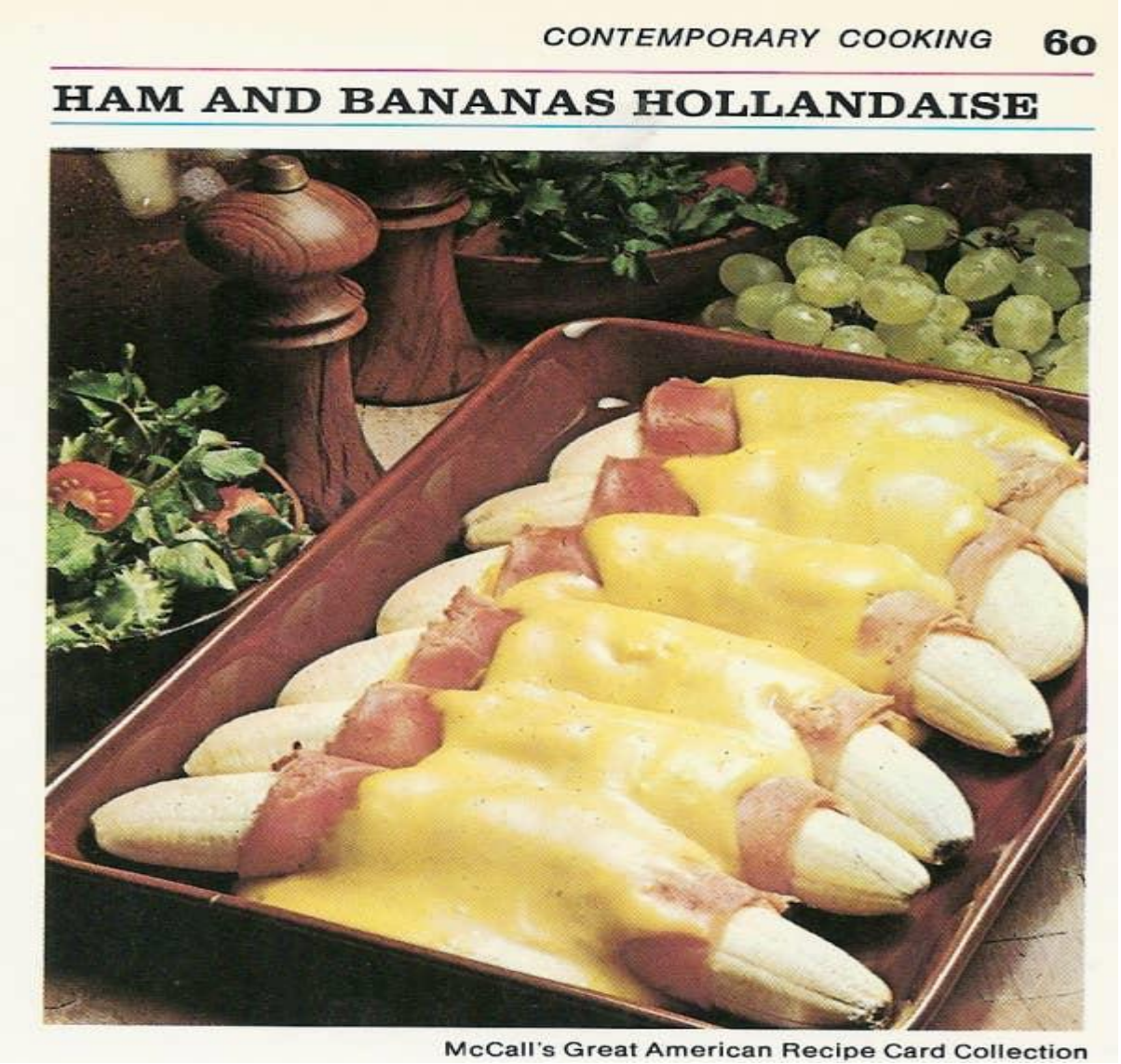
6 medium bananas
1/4 cup lemon juice
6 thin slices boiled ham (about 1/2 lb)
3 tablespoons prepared mustard
2 envelopes (1 1/4-oz size) hollandaise sauce mix
1/4 cup light cream

1. Preheat oven to 400F. Lightly butter 2-quart, shallow baking dish.

2. Peel bananas; sprinkle each with 1/2 tablespoon lemon juice, to prevent darkening.

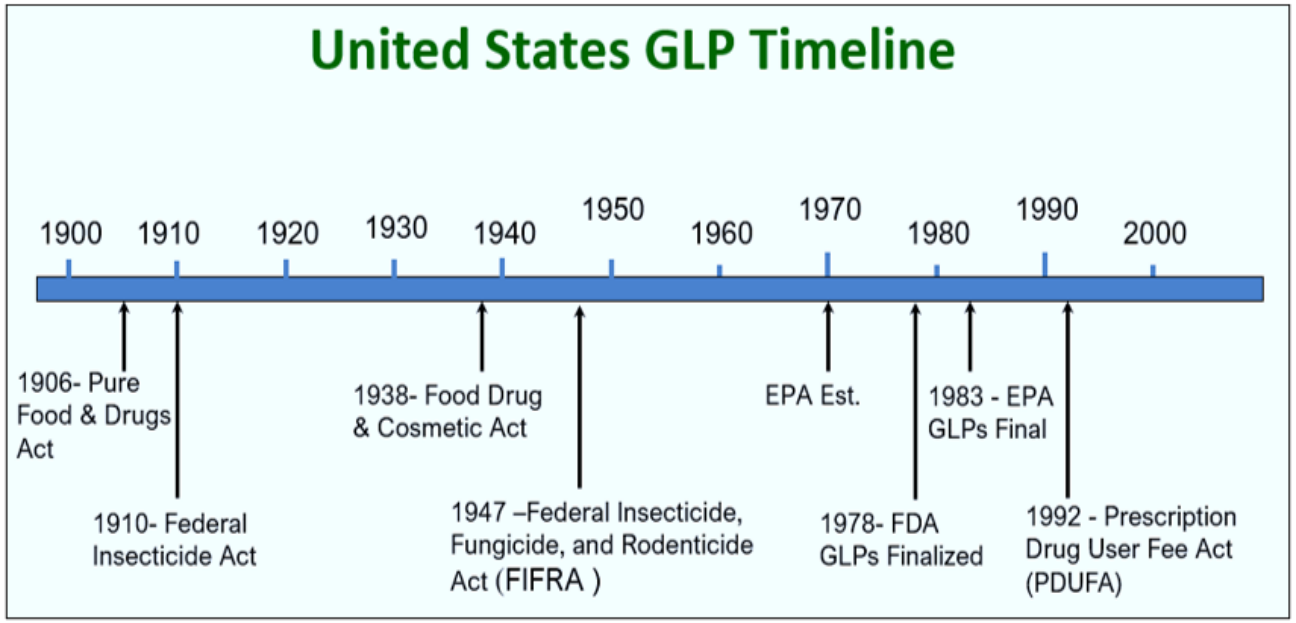
3. Spread ham slices with mustard. Wrap each banana in slice of ham. Arrange in single layer in casserole. Bake 10 minutes.

4. Meanwhile, make sauce: In small saucepan, combine sauce mix with 1 cup water, 1 tablespoon lemon juice, and cream. Heat, stirring, to boiling; pour over bananas. Bake 5 minutes longer, or until slightly golden. Nice with a green salad for brunch or lunch. **Makes 6 servings.**



EPA

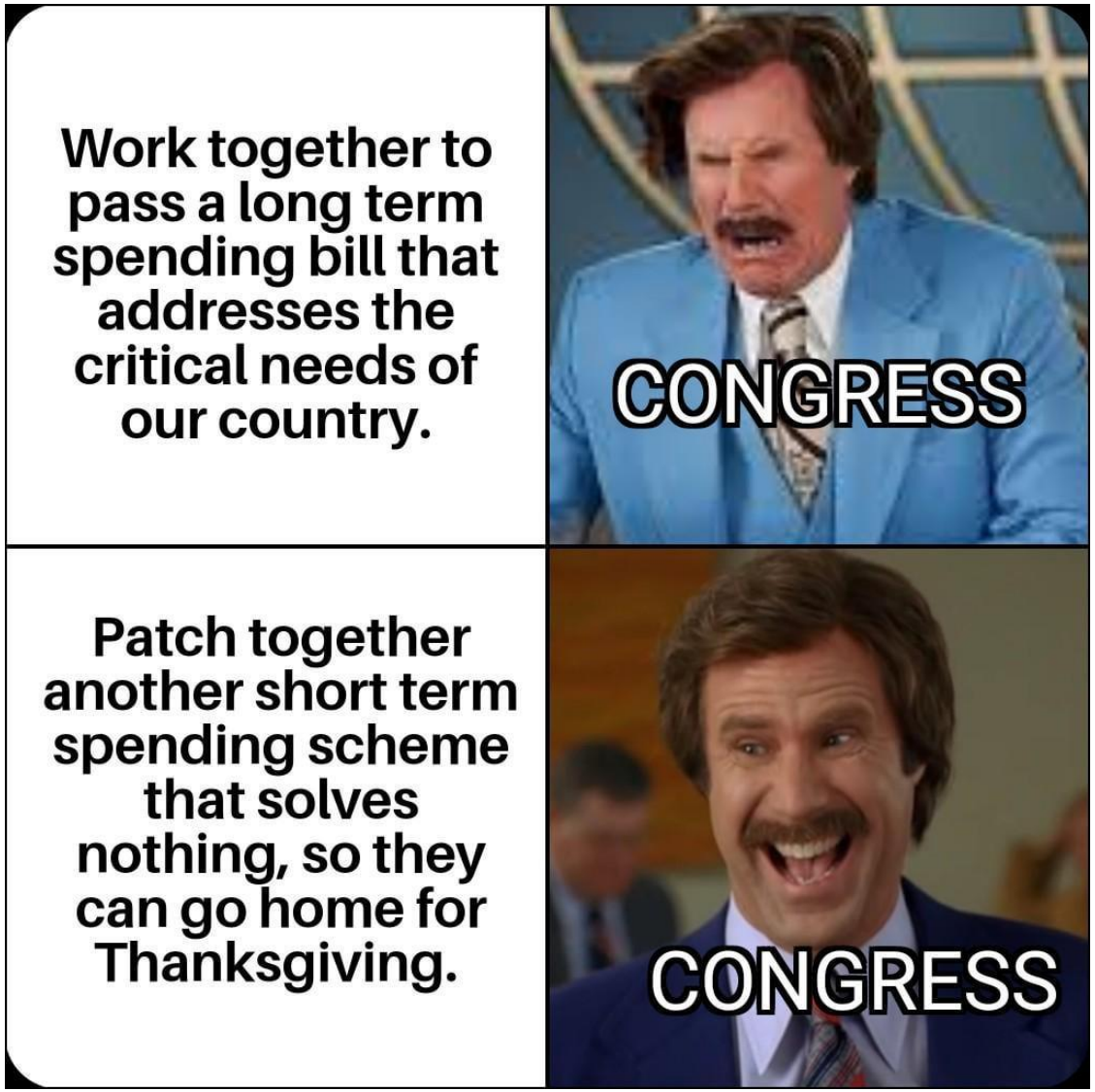
- Federal pesticide legislation enacted in 1910 under USDA authority
- FIFRA became law in 1947
- EPA created in 1970; FIFRA authority shifted from USDA
- Revision of FIFRA in 1972



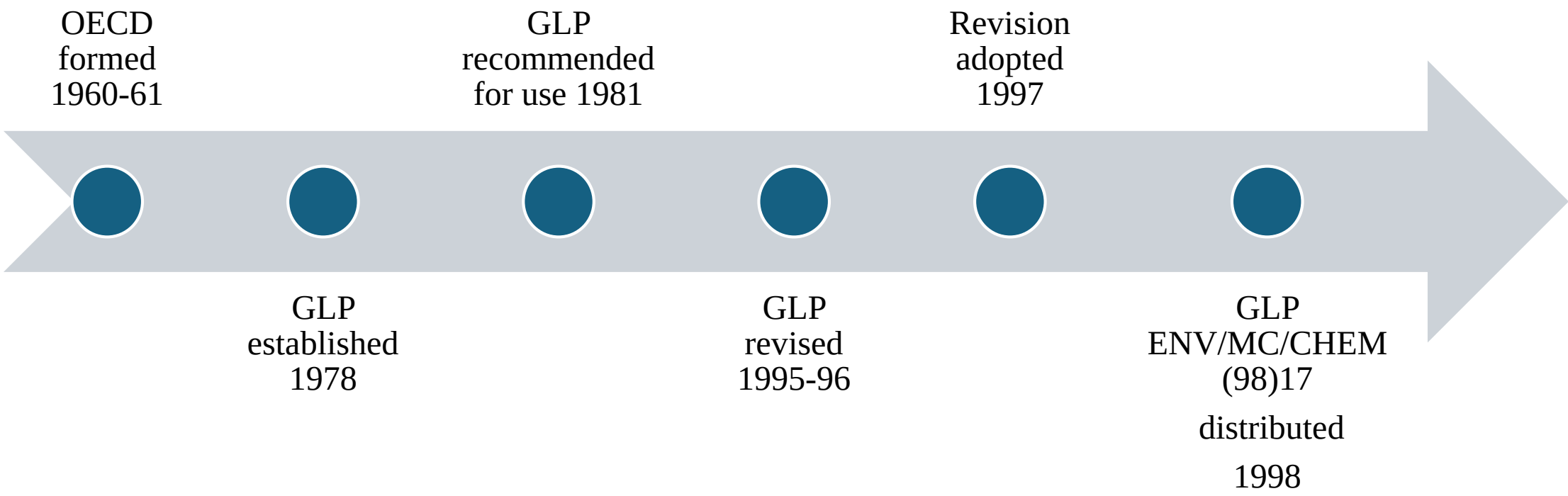
1972	New Zealand introduced Good Laboratory Practice as the Testing Laboratory Registration Act. Denmark also passed a law to promote Good Laboratory Practice.
1975	The FDA received a tip that there were problems with tests submitted by one of its biggest testing partners—Industrial Bio-Test Laboratories (IBT).
1976	A FDA inspection found extensive evidence of fraud and abuse in IBT laboratories. As a result of the investigation, more than 70% of studies audited by the FDA were invalidated. In response, Congress proposed and enacted the Good Laboratory Practice Regulations (GLP) for FDA as part of the Federal Food, Drug, and Cosmetic Act (FD&C).
1978	The Good Laboratory Practice Regulations, Final Rule was published in the Federal Register.
1979	Title 21 Code of Federal Regulations Part 58—Good Laboratory Practice for Nonclinical Studies became law.
1983	EPA proposed Good Laboratory Practice guidelines for pesticide toxicology studies in two parts—Toxic Substances Control Act (TSCA) and Federal Insecticide, Fungicide and Rodenticide Act (FIFRA).
1987	21 CRF Part 58 was amended with GLP changes related to quality assurance, protocol preparation, testing, control article characterization, and retention of specimens and samples.
1989	EPA 40 Code of Federal Regulations Part 160—Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) was enacted. It includes regulations requiring GLP compliance for studies that support or are intended to support applications for research or marketing permits for pesticide products regulated by the EPA.

EPA Fun Fact

- Authorization for appropriations for FIFRA expired on September 31, 1991
- EPA authority not affected



OECD


OECD formed 1960-61
GLP established 1978
GLP recommended for use 1981
GLP revised 1995-96
Revision adopted 1997
GLP ENV/MC/CHEM (98)17 distributed 1998

OECD

Industry is responsible for safe use and production of chemicals

Government ensures Industry responsibility through regulation

GLP developed to promote the quality and validity of test data used for determining the safety of chemicals and chemical products.

GLP required for studies submitted to national authorities for assessment of chemicals

OECD

Principles of GLP aren't legally binding but are legally binding.

Member countries required to have certain procedures and recommended to use OECD GLP principles

For example:

- UK legislation falls under The Good Laboratory Practice Regulations 1999 no. 3106 and includes GLP as based upon Annex 1 of OECD.
- German legislation is under the German Chemicals Act section 6 Good Laboratory Practice - §19a-d as pursuant to Annex 1 of OECD principles.

Supporting Principles of GLP

- Guidelines
- Advisory and Consensus Documents

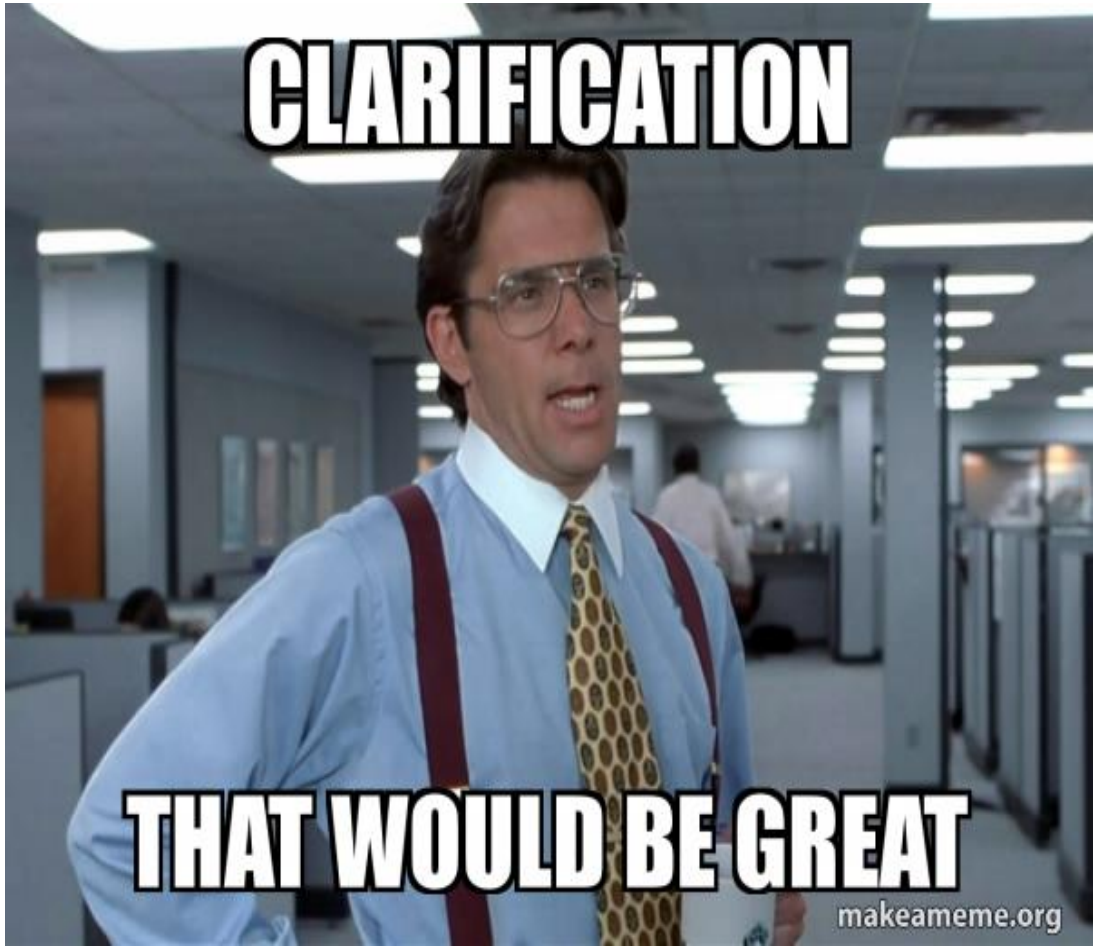
Guidelines - EPA

- Guidelines aren’t regulations
- EPA recommendations
- EPA has 11 series with numerous guidelines in each series
  - Familiar - 850.1600

Guidelines - OECD

- OECD has 5 categories with numerous guidelines per category
- Internationally agreed testing methods
  - Familiar – Sec 5: Test no. 509
- OECD recommends requirement of the recommended guidelines

Advisory and Consensus Documents



- EPA has ~80 advisories
  - Purpose is to provide GLP specific clarification from EPA
- OECD has 18 numbered documents – mix of consensus and advisory
  - Guidance for the application of GLP from consensus workshops or public consultation

Similarities of the Principles

- Resources: organization, personnel, facilities, and equipment
- Characterization and care: test items and test systems
- Rules: protocols and standard operating procedures (SOPs)
- Results: raw data, final reports, and archives
- Quality Assurance: independent monitoring of research processes

Differences

CERTIFICATION

LANGUAGE

DEFINITIONS

RESPONSIBILITIES

APPARATUS/EQUIPMENT

ARCHIVE AND RETENTION

Language

EPA	**OECD**
Test substance	Test item
Control and reference substance	Reference item (“control item”)
Protocol	Study Plan
Experimental termination date	Experimental completion date
Quality Assurance Unit	Quality Assurance Programme
Equipment	Apparatus
Nature of study	Type of study

Definitions

- EPA has 23 –
  - 5 of the EPA definitions are not defined in OECD definitions; these define carrier, control substance (the OECD reference item definition includes (“control item”) beside it), FDA, FFDCA, and FIFRA
- OECD has 25 –
  - 10 of the OECD definitions are not defined in EPA definitions. These define test site, test facility mgt, test site mgt, PI, SOPs, master schedule, short term study, study plan, study plan amendment, and study plan deviation
- EPA is alphabetical and OECD is grouped by category

Definitions Continued…

- Experimental start date – EPA defines it as first date of test substance application whereas OECD defines it as the date when the first study specific data is collected.
- Test Facility – **EPA** defines it as a person who actually conducts a study, *i.e.*, actually uses the test substance in a test system. “Testing facility” encompasses only those operational units that are being or have been used to conduct studies. **OECD** defines it as the persons, premises and operational unit(s) that are necessary for conducting the non-clinical health and environmental safety study. For multi-site studies, those which are conducted at more than one site, the test facility comprises the site at which the Study Director is located and all individual test sites, which individually or collectively can be considered to be test facilities.

Responsibilities

- **TFM** – OECD has more responsibilities listed than EPA has.
- **SD** – OECD lists more responsibilities; EPA specifically states the SD will assure compliance with all GLPs.
- **PI** included in OECD, but not for EPA

Responsibilities Continued...

- **Personnel** – EPA focus is on training and their records, health, and safety whereas OECD discusses personnel being knowledgeable, exercising health precautions, complying with study plan and SOPs, and recording and quality of data

- **QA** – **OECD** requires maintaining copies of SOPs, protocol verification for GLP compliance, requires assurance that personnel have protocol and SOP's, lists the types of inspections to be conducted, promptly report results in writing to Mgt & SD. For **EPA**, it is understood to have SOP's, inspect the protocol for GLP compliance, ensure staff have protocol and SOP's, and the types of inspections needed. EPA lists that Mgt and SD has to be contacted immediately for study integrity issues.

Apparatus/Equipment

- EPA gives more detail on what should be included in equipment SOP’s and requires written documentation of maintenance.
- OECD states calibration should be traceable to a national or international standards of measurement.

Archives/Retention Times

- EPA requires study archival on or at time of study completion.
- OECD requires archival after study completion.
- EPA GLP lists specific retention times.
- OECD doesn’t provide specific retention times, but rather leaves it up to the governing countries regulating authorities.

Closure

References

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- U.S. EPA Pesticide Registration - REACH24H Consulting Group
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- Fundamentals of Laboratory Management | OER Commons
- OECD Principles on Good Laboratory Practice (GLP) (nih.gov)
- OECD Principles on Good Laboratory Practice | OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring | OECD iLibrary (oecd-ilibrary.org)
- The Mutual Acceptance of Data (MAD) System | OECD
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