

# Identifying Surrogate Environments to Meet Local Field Trial Requirements



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TOKYO, NOVEMBER 2018

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# Conflict of Interest and Funding Source Disclosure



The speaker declares no conflict of interest related to this presentation

Scientific work described in this presentation was funded under three separate grants from USDA Foreign Agricultural Service

Support for speaker travel comes from ILSI Japan and a discretionary grant to ILSI Research Foundation from CroLife International

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# Contents of the Presentation



What is a Surrogate?

- Why is this useful for regulation?

Can we identify surrogate environments for Confined Field Trials(CFTs)?

- (I think the answer is “yes”)

Using a surrogate approach to satisfy CFT requirements

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# What is a Surrogate?



Merriam-Webster Dictionary

- “one appointed to act in place of another”
- “A substitute”

In regulation, this is typically a surrogate organism

- Intended to substitute for humans or other species that are difficult to test in the laboratory



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## Surrogates in Regulation

The use of surrogate species is well accepted for many regulatory purposes

- Drug and pharmaceutical evaluations
- Chemical and pesticide testing

Regulatory decision making would not be possible in these areas without use of surrogates for testing

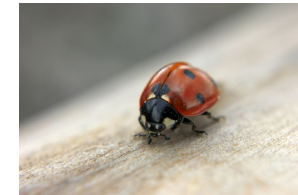
This acknowledges two realities

- You can't test everything directly
- Although a surrogate will never be identical to the species you care about, an appropriate surrogate is adequate to ensure safety

## Identifying Surrogates for Regulatory Testing

The surrogate must be an appropriate substitute for the purpose of the test

- Demonstrate similarity to the species/subject of interest
- Show similar responses or share parameters that are relevant for the test result



Therefore, you need to understand your test in order to know if you have an appropriate surrogate



## Can we identify surrogate environments for Confined Field Trials(CFTs)?

The surrogate environment approach is already applied in the conduct of CFTs

- Small scale trials are extrapolated to draw conclusions about cultivation in a much larger environment

However, many countries require in-country testing to support regulatory assessments of GE plants

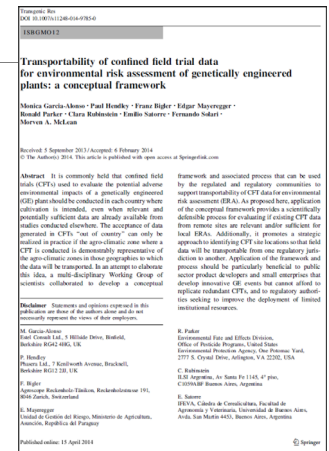
- Although political boundaries are not parameters that influences the test results

## What are the relevant parameters of a CFT environment?

If we want to identify surrogate environments, we first need to understand the tests being performed

- What are we testing in CFTs?

Then we need to consider the characteristics of the environment that may influence the results of those test



## CFTs are comparative assessments

GE PLANT



Observations

- Growth Rate
- Reproduction
- Pest Suscept.
- Disease Suscept.
- Physical characteristics of the plants

CONVENTIONAL COMPARATOR



## What are the components of the Environment?

Biotic: all the living things

- Microorganisms
- Macroorganism

Abiotic

- Weather
- Climate
- Physical Characteristics



## Confined Field Trial Data

DATA TYPICALLY ADDRESSES

**Agro-phenotypic characteristics**

- Collected primarily for unintended effects assessment
- To verify there are no changes in reproductive or growth habits

**All the data is comparative**

- With one or more comparators grown in the same trial
- Or to known reference varieties

DATA TYPICALLY DON'T ADDRESS

**Biodiversity interactions**

- Biotic interactions are pretty tightly controlled under field trial conditions
  - Part of the confinement protocol
- Sometimes arthropod surveys are done – these are generally less informative than laboratory data

Most of the informative data for assessing risk to biodiversity is laboratory data or from published literature

## So an appropriate surrogate environment

Should be one where we would expect pair-wise comparisons between a GE crop and the conventional parent (or other comparator) to yield the same results.

The ecology of the site should not matter

- Because it will be an agricultural environment under confinement conditions
  - Limiting biological interaction
- Diseases and pests will be controlled because they interfere with the results of the pair-wise comparison

Demonstrating a similar physical environment should be enough to establish an appropriate surrogate environment for CFTs

## Demonstrating Similarity in the Physical Environment



Identify an appropriate surrogate environment using characteristics of the physical environment

There are many ways you might do this:

- Any location that can grow a crop arguably shares physical characteristics that are relevant to the results of a CFT
- It may be enough simply to know that you can grow the crop of interest in both locations
- Agro-climate similarity
  - A measure of physical characteristics including, for example, growing degree days (GDD) seasonality, high and low temperatures etc.
  - Provides a scientifically defensible rationale for asserting that the environments are substantially the same

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## Agroclimate



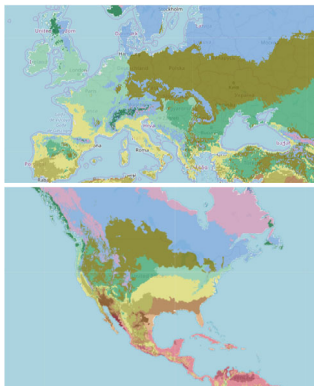
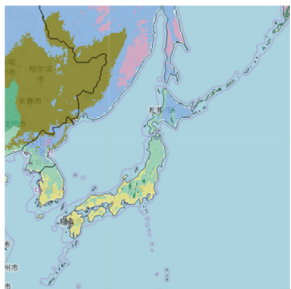
There are many different Agroclimate zonations available

We have chosen to use the Global Environment Stratification (GENS)

- Publicly available
- Zonation is hierarchical
- Built on data from publicly available sources
  - Not based on mathematical modeling
- Compares favorable with other zonations
  - (see van Wart et al. 2013)

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## Agroclimate Visualization Using the Global Environment Stratification (GENS)



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## Practical Application



Rational planning for the conduct of field trials

- Selecting field trial sites that occupy an agroclimate zone with relevance for countries where future risk assessments will be conducted

Satisfying “in-country” field trial requirements with data generated in surrogate environments outside of the country

- Either in one or multiple countries/locations where trials have been previously conducted

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## What else is required?

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Regulatory authority must be interested/willing to meet data requirements with remotely collected data

- Legal or regulatory requirements are not always amenable to a scientific rationale
- Countries may perceive some other benefit to conducting in country trials

If a country is willing to use data collected from surrogate environments, those data must be collected in compliance with regulatory requirements

- Requirements need to be transparent, and determined in advance

Specific, hypothesis driven testing in a given environment may still be warranted

- Provided there is a plausible pathway to harm and the experiment being done is able to provide useful information

## Conclusions

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It is possible to apply a surrogate approach to make use of remote environments to satisfy local field trial requirements

Pre-requisites for using the surrogate environment approach:

- Establish that the environment where the trials are conducted is relevant in the country where the data is intended to be used
  - This is where the agroclimate data are useful
- Harmonization of protocols for CFTs
  - Ensuring that the data being collected are in conformance with regulatory requirements wherever they might be used
- Document that the trial was conducted properly and there are no anomalies in weather or other externalities that would impact the trial results

## Thank You!

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### References

1. Van Wart, J. *et al.* Use of agro-climatic zones to upscale simulated crop yield potential. *F. Crop. Res.* **143**, 44–55 (2013).
2. Garcia-Alonso, M. *et al.* Transportability of confined field trial data for environmental risk assessment of genetically engineered plants: a conceptual framework. *Transgenic Res.* 1025–1041 (2014). doi:10.1007/s11248-014-9785-0