Infinitely better method transfer

Agilent 1290 Infinity with Intelligent System Emulation Technology (ISET)
Agenda

• Method transfer workflows
• Parameter affecting instrument to instrument method transfer
• Current solutions
• What is ISET
• Performance examples
• Summary
Method Transfer Workflow

Location A

Discovery -> Development -> Quality Control

Regulated environment

Location B

Discovery -> Development -> Quality Control

Regulated environment
Method Transfer Workflow

**Location A**

- Discovery
- Development
- Quality Control

*Regulated environment*

**CRO**

- Development
Method Transfer Workflow

Location A

Discovery → Development → Quality Control

Regulated environment

CMO

Regulated environment

Quality Control
Method Transfer Workflow

Methods from Literature:
Scientific journals, application notes, etc

Instrumentation:
1100 Series, 1200 Series, Alliance, Acquity, etc
Design Differences (U)HPLC Systems

• Delay volumes (gradient formation)
• Power range (flow x pressure)
• Extra column volume
• Temperature
• Data rates
• Sensitivity

Problem:
Instrument to Instrument Method Transferability
• Not possible
• Requires Re-development
• Requires Re-validation

Resulting in huge additional cost factor:
Instrument to Instrument Method Transferability
- Important Parameters

- **Pump**
  - Delay volume
  - Gradient mixing behavior
  - Pressure x flow rate
  - Retention Time
  - Resolution

- **Sampler**
  - Delay volume
  - Extra column volume
  - Injection volume
  - Retention Time
  - Resolution
  - Sensitivity

- **Column Thermostat**
  - Temperature profile
  - Extra column volume
  - Retention Time
  - Resolution

- **Detector**
  - Data rate
  - Extra column volume
  - Path-length
  - Resolution
  - Retention Time
  - Sensitivity
Instrument to Instrument Method Transferability

- Important Parameters

- Delay volume
- Gradient mixing behavior
- Flow rate & pressure
- Retention Time
- Resolution

- Delay volume
- Extra column volume
- Retention Time
- Resolution

- Injection volume
- Sensitivity

- Temperature profile
- Extra column volume
- Retention Time
- Resolution

- Data rate
- Extra column volume
- Path-length
- Resolution
- Retention Time
- Sensitivity
Instrument to Instrument Method Transferability
- Impact of delay volume and mixing behavior

What happens with a programmed gradient?

response

90%

10%

time

Programmed gradient step
1200 Series Binary Pump SL
1290 Infinity Binary Pump

Gradient slope/
Mixing behavior

Delay
volume

Total delay volume of the system
(sum of capillaries, mixer, cells, valves..)
Gradient Analyses with Different LC Systems

- Impact of delay volume and mixing behavior

**The result:**
- Difference in RT and Resolution
- One peak is missing!

Sample: 0.5% impurities in formulation (metoclopramide)
Xbridge C18, 150x3 mm, 3.5 µm dp,
0.45 ml/min, Eluent: A =0.25 % AmAc, B = ACN,
Gradient: 0-15 min; 5-57 % B
Instrument to Instrument Method Transferability

- *What can you do today?*

• From a *lower to higher* dwell volume LC system
  
  A) Adding physical volume (plumbing solution)  
  B) Modifying your gradient table with isocratic hold

• From a *higher to lower* dwell volume LC system
  
  C) Delay the injection (see appendix)
Method Transfer Possibilities Today

- A) Adding physical volume (plumbing solution)

Example: 1290 Infinity LC

1290 + 1000 μL dwell vol.

1100/1200 Quat Pump
Method Transfer Possibilities Today
- A) Adding physical volume (plumbing solution)

Example: 1290 Infinity LC

1290 + 1000 μL dwell vol.

1100/1200 Quat Pump

Advantages
- Works well for not so fast analysis
- No Method change

Disadvantages
- Requires hardware change, no flexibility
- Requires manual determination of the dwell volume (Pumps with damper the dwell volume is not constant and depends on pressure)
- Hardware change difficult in validated environment
Method Transfer Possibilities Today

- B) Isocratic Hold

Example: 1290 to 1200

Isocratic hold: move the gradient

Programmed gradient
1290 gradient
1200 gradient
Method Transfer Possibilities Today

- B) Isocratic Hold

Example: 1290 to 1200

Does not consider the gradient mixing behavior (different curves).
Method Transfer Possibilities Today

- **B) Isocratic Hold**

Example: 1290 to 1200

1. **1200 Series LC Binary Pump**
2. **1290 Infinity LC + 860 µl “Delay Volume”**
3. **1290 Infinity LC + 900 µl “Delay Volume”**
4. **1290 Infinity LC + 940 µl “Delay Volume”**
Method Transfer Possibilities Today

- B) Isocratic Hold

Example: 1290 to 1200

**Advantages**
- Flexible, *Isocratic Hold* is part of the method

**Disadvantages**
- Works not in all cases
- Requires manual determination of the dwell volume/isocratic hold (Pumps with damper the dwell volume is not constant and depends on pressure)
- Requires modification of the methods (should be avoided in validated environment, but doesn’t require revalidation USP Chapter <621>)

[Graph showing 1260 Infinity LC and 1290 Infinity LC with 900 µl hold]
NEW

Intelligent System Emulation Technology (ISET)

The Solution
What is ISET?

- **Two components**

A. Best in class performance of the 1290 Infinity LC
   Broad power range, ultra-low delay volume, superior sensitivity, unmatched flow and composition accuracy

B. The revolutionary ISET emulation algorithm
   Full characterization of target LC systems
   Creation of emulation function
Method Transferability: 1290 Infinity LC
- System Emulation Technology

Concept

Select System to be emulated by a simple mouse click:

- Agilent 1100 Series
- Agilent 1200 Series LC
- Agilent 1260 Infinity LC
- Agilent 1220 Infinity LC
- Other
Intelligent System emulation technology
- How it works (1290 to 1200)

Same gradient conditions by moving the gradient and by emulating the gradient mixing behavior.
Pesticides

Column: 3 x 50 mm, 2.7 µm Poroshell

1290 Infinity LC with iSET

1290 Infinity LC

1100 Series Binary LC

Rs = 1.87

Rs = 1.15

Rs = 1.90

mAU

800

700

600

500

400

300

200

100

0

1 1.5 2 2.5 3 3.5 min

Metamitron

Chloridazone

R_s = 1.87

Cyanazine

Simazine

Chlortoluron

Diuron

Propazine

Terbutylazine

Prometryn
Impurities analysis

Column: 4.6 x 50 mm, 1.8 µm

Rs = 3.29

Rs = 2.92

Rs = 3.23

1290 Infinity LC with iSET

1290 Infinity LC

1100 Series Binary LC
Advantages

- Simple and flexible
  (select the emulated LC system simply by a mouse click)
- No determination of the dwell volume etc. required
  (perfectly covers pumps with damper and not constant dwell volume)
- Works perfectly in all cases
- Requires no modification of the methods
  (no conflicts in regulated environment)
Intelligent System Emulation Technology ISET

- Benefits

▸ Accelerate your method transfer
  No more method transfer problems! Simply emulate the LC system on which the original method was developed—with a single mouse click.

▸ Make a safe investment
  Run your legacy methods with ISET and at the same time take full advantage of the UHPLC speed, resolution and sensitivity of the 1290 Infinity LC.

▸ Achieve higher productivity
  Speed up your method development with UHPLC performance and then fine-tune your method by emulating the target system—and be confident that the method will run as intended.
Agilent 1290 Infinity LC with ISET inside

- The Art of Emulation

- Emulates other (U)HPLC instruments
  - by a simple mouse click

- Runs existing (U)HPLC methods
  - without modifying method or system

- Delivers same retention times and peak resolution
  - for infinitely better method transfer