Intelligent System Emulation (ISET): New Possibilities in the Field of Method Development and Further Applications

Heike Wächtler, Monika M. Dittmann, Konstantin Choikhet, Klaus Witt, Gerhart Metzler

HPLC 2013
INST26_TU

Agilent Technologies

Introduction

Due to the introduction of UHPLC instruments to the market in the past few years the instrument-to-instrument method transferability has become an increasingly important topic.

Significant differences between UHPLC and HPLC systems can lead to notable changes in retention times and often in selectivity when methods developed on standard HPLC systems are run on modern UHPLC systems or vice versa.

As in many laboratories HPLC systems are slowly exchanged by UHPLC systems, an important requirement is the opportunity to transfer methods between labs of different divisions/locations, where various types of HPLC systems are used to develop methods as well as to carry out analytical measurements.

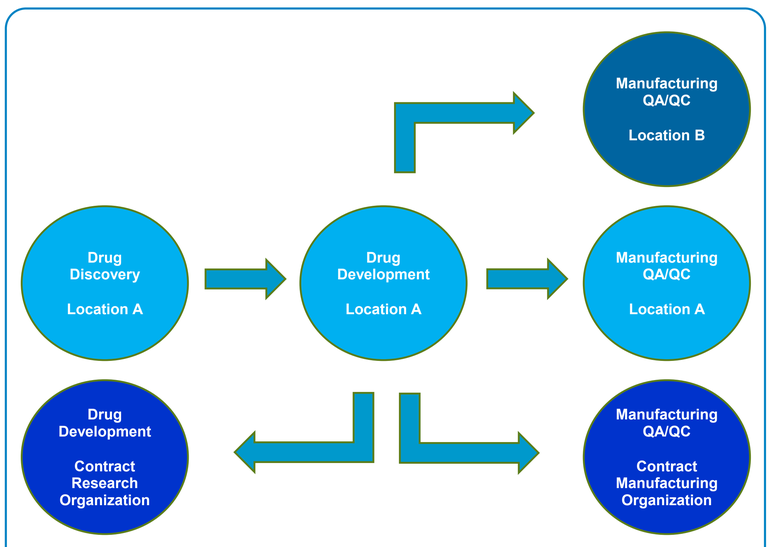


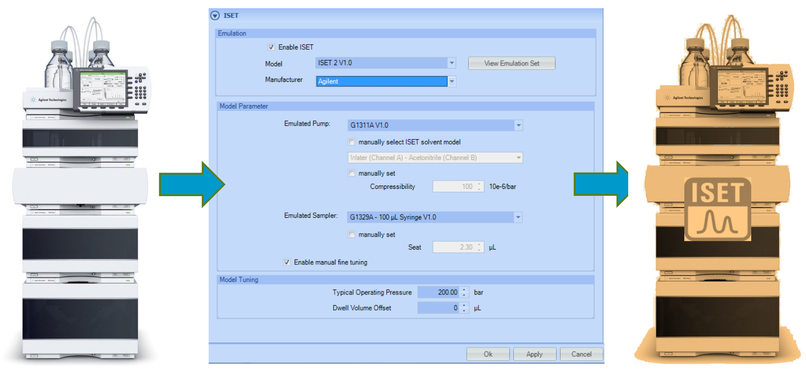
Figure 1: The transfer of analytical methodology between research and development departments, contract research organizations, and manufacturing is an essential step in the development of a new pharmaceutical product. Different workflows utilized in the pharmaceutical industry are shown.

The common approaches to overcome this problem are usually not feasible or practicable. This is particularly true in a compliance controlled environment.

Intelligent System Emulation (ISET) was introduced to the market recently. It provides the transfer of existing methods from standard HPLC to a UHPLC system; this includes gradient formation properties. It also offers method development or robustness tests for different HPLC/UHPLC systems carried out on just one UHPLC instrument that is equipped with ISET.

Furthermore, the usage of ISET entirely intuitive even though it provides extensive configuration capabilities.

Easy-click method transfer

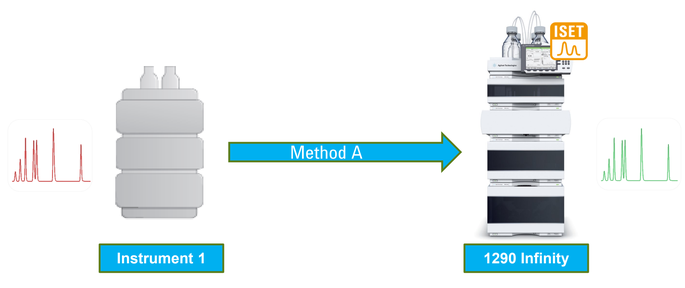


In the following are some applications presented in order to demonstrate the various use cases.

Workflows

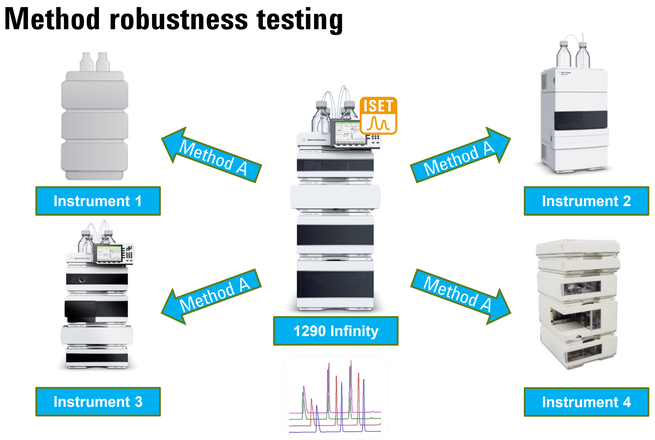
ISET offers in principle three options for instrument to instrument method transfer:

Perform legacy methods/existing methods



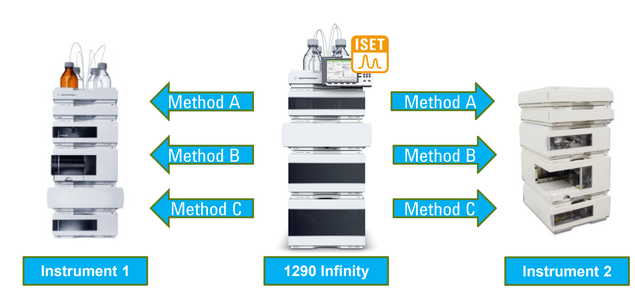
Perform already existing methods on the 1290 Infinity instrument without change in retention times and resolution

Method robustness testing



Testing a method for robustness against variation in instrument characteristics using just one instrument.

Method developement



Develop methods for a variety of instrumens on one 1290 Infinity instrument while maintaining individual instrument characteristics

Perform existing methods

The range of instruments that can be emulated by ISET is continually extended in order to simplify the transfer of most of the existing methods to 1290 Infinity binary and quaternary systems. Figure 2 shows a method transfer from a Non-Agilent UHPLC system to a 1290 Infinity binary system by using ISET.

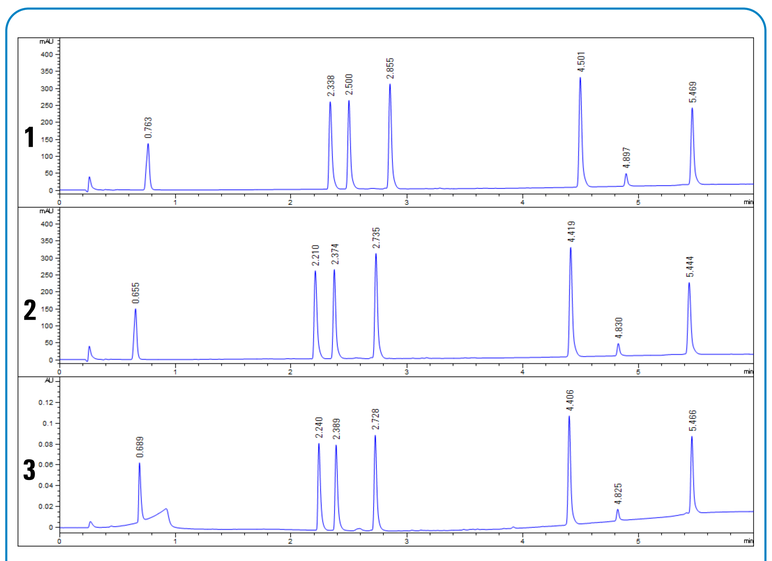


Figure 2: Gradient runs of a GSK Test mixture [1] performed on (1) 1290 Infinity system, (2) 1290 Infinity system in emulation mode for Non-Agilent UHPLC system and (3) Non-Agilent UHPLC system. Method: (A) gradient water + 0.1% TFA-acetonitrile + 0.1% TFA 3-100% in 5 min, flow rate 1.0 ml/min, 3.0x50 mm Zorbax SB-C18, 1.8 µm column, 30°C.

Sample (in order of elution): 8-Bromoguanosine, amitryptyline hydrochloride, 4-chlorocinnamic acid, di-ethyl phthalate, di-amyl phthalate, di-n-hexyl phthalate, di-octyl phthalate

Robustness Test

An earlier aproach to eliminate inter-laboratory transfer problems is robustness testing. It is used to indicate the capacity of an analytical method to be unaffected by small but deliberate variations in method parameters like pH and temperature.

Because of strict regulatory requirements it is mainly performed for pharmaceutical analyses and became an important part of method validation or method optimization.

Apart from test conditions such as temperature, different days or different analysts, the specific characteristics of various HPLC/UHPLC instruments have a high impact on method transferability. ISET offers the possibility to perform robustness testing also with respect to diversity of several HPLC instruments while using just one UHPLC instrument.

Figure 3 demonstrates a robustness test carried out with a 1290 Infinity System emulating four different HPLC instruments.

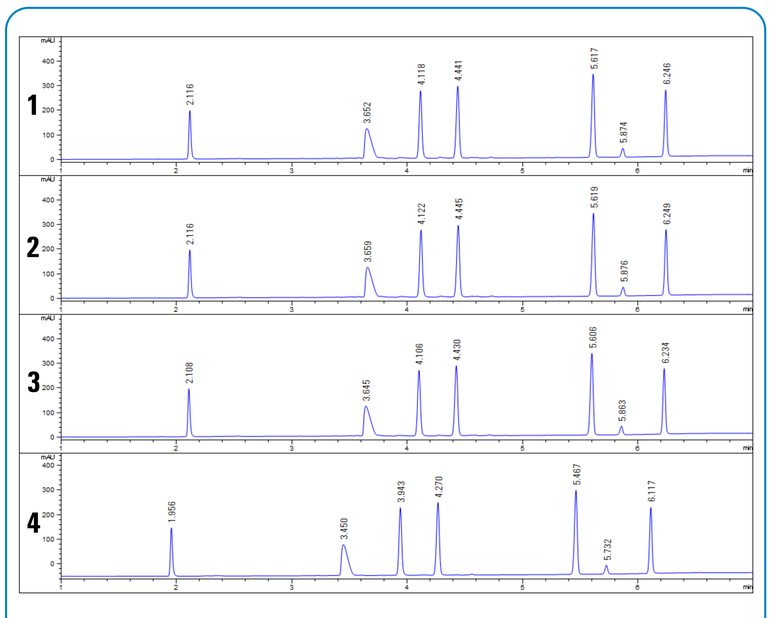


Figure 3: Gradient runs of a GSK Test mixture [1] performed on 1290 Infinity system in emulation mode for (1) 1200 binary pump (G1312B) + G1367A auto sampler, (2) 1100 binary pump (G1312A) + G1367A auto sampler (3) 1200 quarternary pump G1311B + G1367A auto sampler and (4) Non-Agilent HPLC system. Method: (A) gradient water + 0.1% formic acid-acetonitrile + 0.1% formic acid 3-100% in 5 min, flow rate 2.0 ml/min, 4.6x100 mm Zorbax Eclipse Plus Phenyl-Hexyl, 3.5 µm column, 254 nm, 25°C.

Method development

Another day-to-day use case is method development. ISET enables the user to establish a method for a variety of HPLC/UHPLC systems with just one instrument. Thus, it is not only possible to shorten the time frame but also to reduce the required instrument resources to a minimum.

Figure 4 depicts the performance of ISET utilized for the development of seperation conditions of a pesticide sample. Emulated data include different types of instruments.

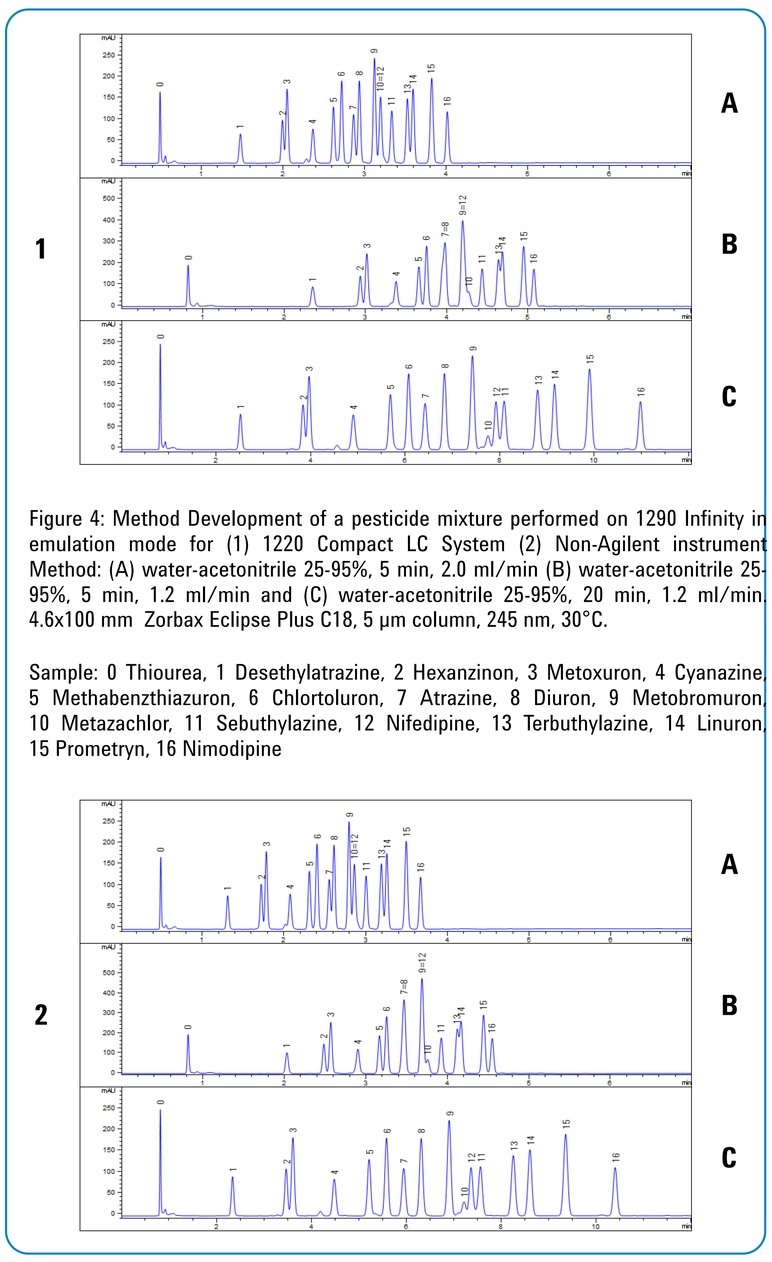


Figure 4: Method Development of a pesticide mixture performed on 1290 Infinity in emulation mode for (1) 1220 Compact LC System (2) Non-Agilent instrument Method: (A) water-acetonitrile 25-95%, 5 min, 2.0 ml/min (B) water-acetonitrile 25-95%, 5 min, 1.2 ml/min and (C) water-acetonitrile 25-95%, 20 min, 1.2 ml/min, 4.6x100 mm Zorbax Eclipse Plus C18, 5 µm column, 245 nm, 30°C.

Sample: 0 Thiourea, 1 Desethylatrazine, 2 Hexanzinon, 3 Metoxuron, 4 Cyanazine, 5 Methabenzthiazuron, 6 Chlortoluron, 7 Atrazine, 8 Diuron, 9 Metobromuron, 10 Metazachlor, 11 Sebuthylazine, 12 Nifedipine, 13 Terbuthylazine, 14 Linuron, 15 Prometryn, 16 Nimodipine

Conclusions

The transfer of analytical methodology between R&D, contract research organizations and manufacturing as well as between different locations of one company is an essential part in the development of a new product.

ISET provides an easy-to-use solution for this requirement with regard to various use cases:

- perform existing methods
- develop new methods
- test a method for robustness

[1] I. Mutton, B. Boughtflower, N. Taylor, D. Brooke, J. Chromatography A 1218 (2011) 3711-3717