Use of Pilot Engineering Systems to model representative manufacturing processes for pesticide active ingredients

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Introduction

For registration of a new pesticide active ingredient, representative batches are prepared. Since it is unrealistic to build and operate an industrial scale manufacturing facility for the preparation of these batches, regulatory agencies accept that batches can be produced using a pilot plant production system.

This poster presents "How" the material is prepared is more important than a prescribed scale of minimum mass or volume, ideally using a system design that most closely models process and operating constraints anticipated at commercial scale.
The concept of a Pilot Engineering System as an effective alternative to a conventional pilot plant system is introduced

SANCO 11802 1.8. Method of manufacture (synthesis pathway) of the active substance

Where the required information is provided for a **pilot plant production system**, that information shall again be provided once industrial scale production methods and procedures have stabilised. Where available, industrial scale data shall be provided before approval under Regulation (EC) No 1107/2009. **Where data on industrial scale production are not available, a justification shall be provided.**

Objective

Pilot plant data is an accepted approach for demonstrating scale-up. Critical to any approach for modeling the production system is to employ a processing system capable of:-

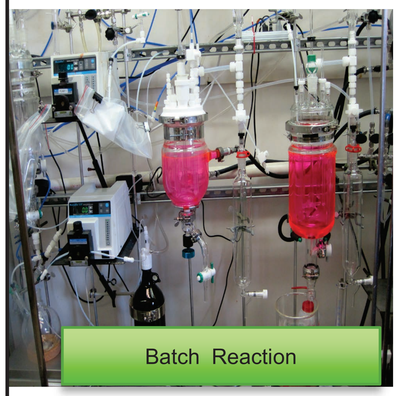
- Generating meaningful data from which an industrial scale manufacturing plant can be designed;
- Enabling modeling of the range of process variability and of potential product impurities, likely to be encountered in the production process.

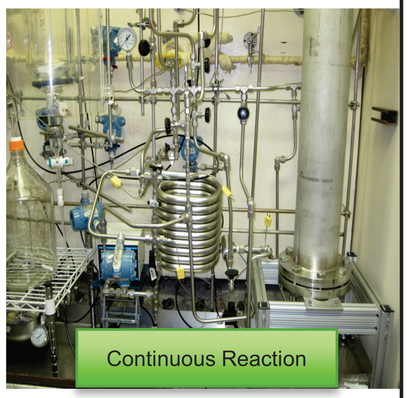
Herein, the concept of a "Pilot Engineering System" (PES) is introduced, at a scale which allows these two objectives to be achieved.

Potential limitations of conventional pilot plant

- Equipment not easily adapted to configuration needed to mimic commercial design
- Capability to recycle solvents and catalysts may be limited
- Materials of construction may not be suited to the process and may have adverse affects on impurities

Examples of Pilot Engineering Systems


Batch Reaction


Continuous Reaction


Distillation


Filtration

Benefits of a "Pilot Engineering System"

+ Defined as 2-30 liter scale, batch or continuous
+ Equipment is more flexible and easily configured to simulate the expected manufacturing process
+ Scaling parameters involving heat & mass transfer, such as reagent addition time, distillation time, reactor residence time, and mixture heating / cooling cycles can be controlled to model manufacturing scale
+ Solvent and reagent recycles, which can impact impurity profile, are easily incorporated in the preparation of the typical batches
+ Process can be contained in a fume hood to minimize risk of exposure to hazardous chemicals
+ Easier to safely test process boundaries
+ Equipment control systems and data acquisition capabilities are highly sophisticated, allowing efficient management of process operating conditions
+ Experience shows that full scale manufacture can be successfully modeled with the PES approach

Conclusions

Manufacturing new pesticide active ingredients in compliance with all regulatory requirements is the desire, intent, and obligation of every ethical agricultural chemical company.

The ability to accurately and robustly model the capability of the eventual, mature manufacturing process during typical batch preparation is an objective shared by both the global regulatory agencies and the manufacturer.

Pilot engineering systems can be an effective alternative to conventional pilot plant production systems. They effectively represent the process capability and enable a product specification to be set for new pesticides that best reflects the variability likely to be observed during industrial manufacture.

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