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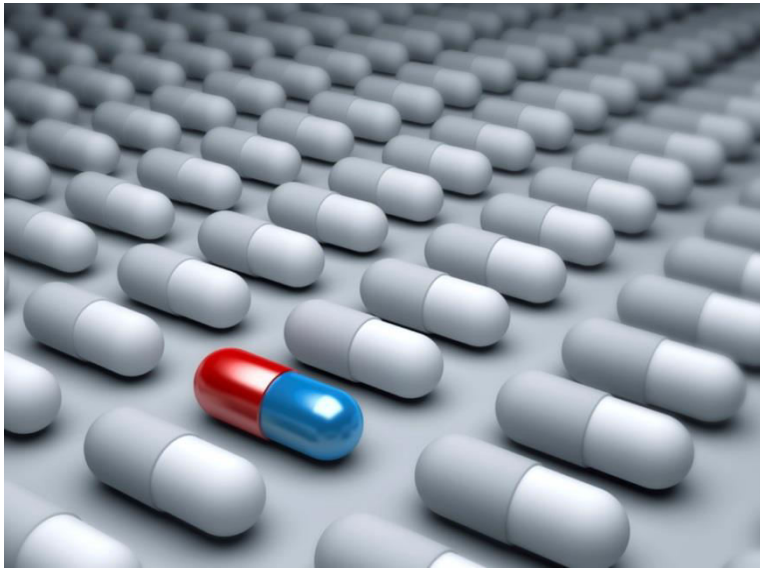
sotax pharmatron Dr. Schleuniger®

Dissolution testing automation: Principles and benefits

Disso India_Mumbai June 2017

- **The pharmaceutical market challenges**
- Some drawbacks of “non-automation”
- Automation principles
- Automation benefits



Challenges of the pharmaceutical market: Patient centricity

We all belong to the pharmaceutical market bringing in our dreams and our fears…

From Reuters

Challenges of the pharmaceutical market: Regulation harmonization

…therefore the pharmaceutical market is tempting to harmonize regulation constraints

Data integrity

Biowaver

Guidelines

ICH
harmonisation for better h

Inspection

21 CFR part 11

USP

PIC/S

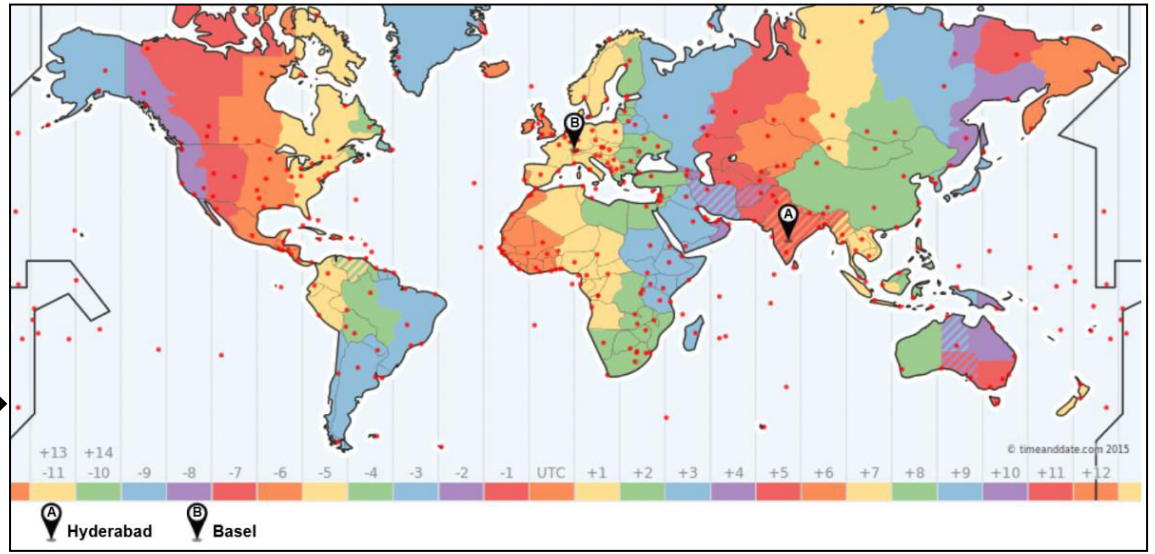
Methods
Databases

Monographs

Moving geographically with markets and their associated cost pressures

R&D

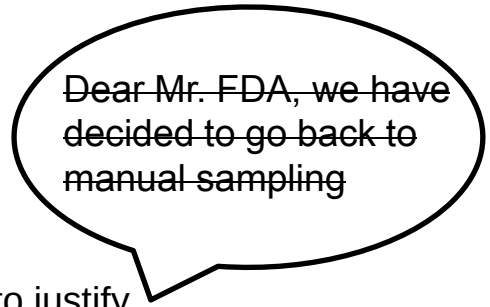
QC



Challenges of the pharmaceutical market: Mergers and Acquisitions

Keeping sustainable tools with objectivity

- The most efficient
- The most advanced
- The less risky



- The easier to justify

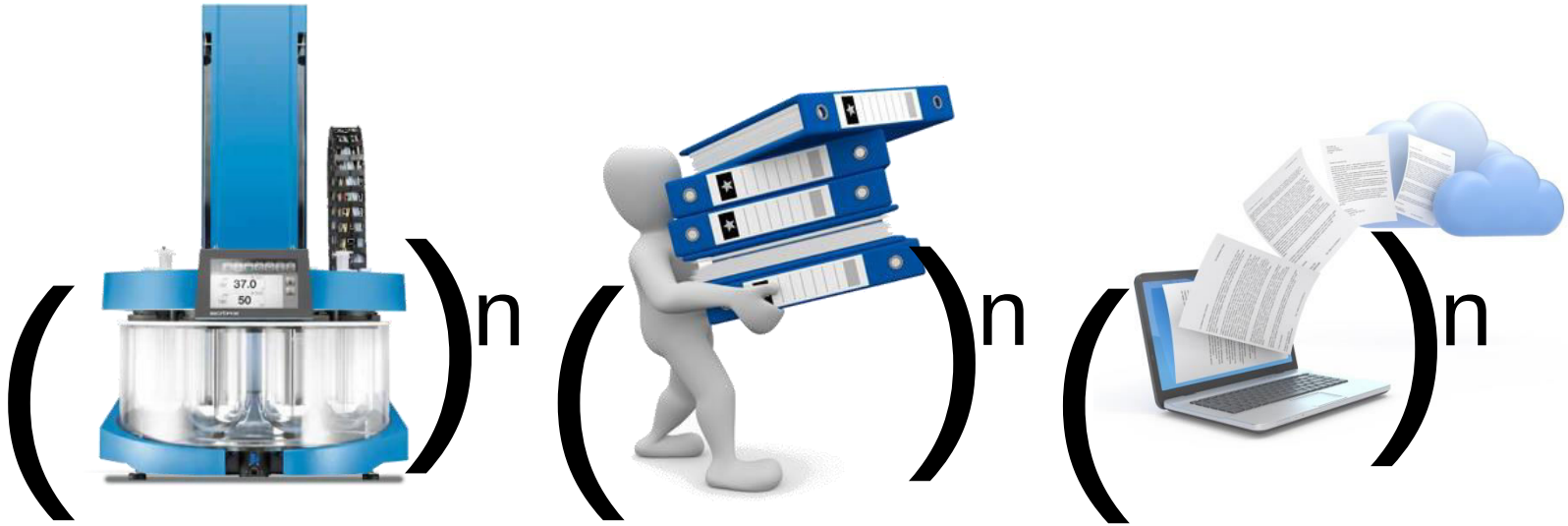
Challenges of the pharmaceutical market: Big Data & AI paradox

Unemployment

Health

- Challenges of the pharmaceutical market
- **Some drawbacks of “non-automation”**
- Automation principles
- Automation benefits

- Multiplication of instruments = multiplication of documents, certificates, procedures, qualification work.



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Increasing manpower

Plus

Cooperation
Trust
Dialogue
Communication
Support
Motivation
Team spirit
Company culture

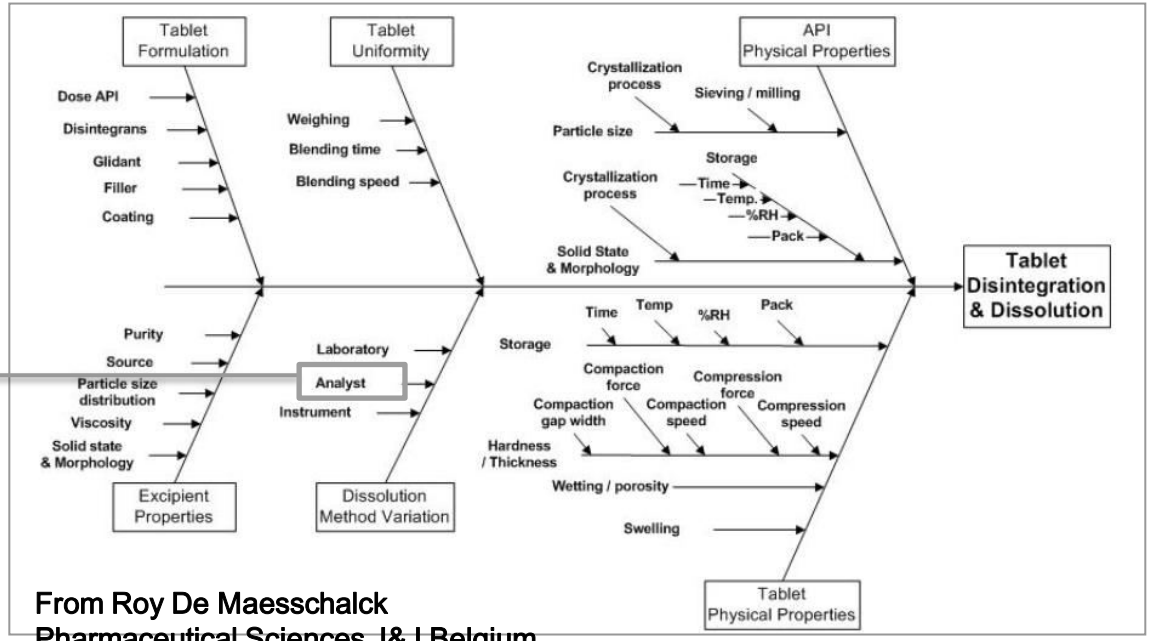
New cost

Organization
Logistics
Middle Management
Supervisors
Meetings
SOPs
Education

Minus

Misunderstanding
Tension
Defiance
Jealousy
Frustration
Segregation by experience
Comfort zones
Overzealessnous

A small part of a big process

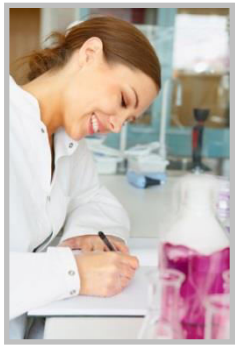


From Roy De Maesschalck
Pharmaceutical Sciences J&J Belgium

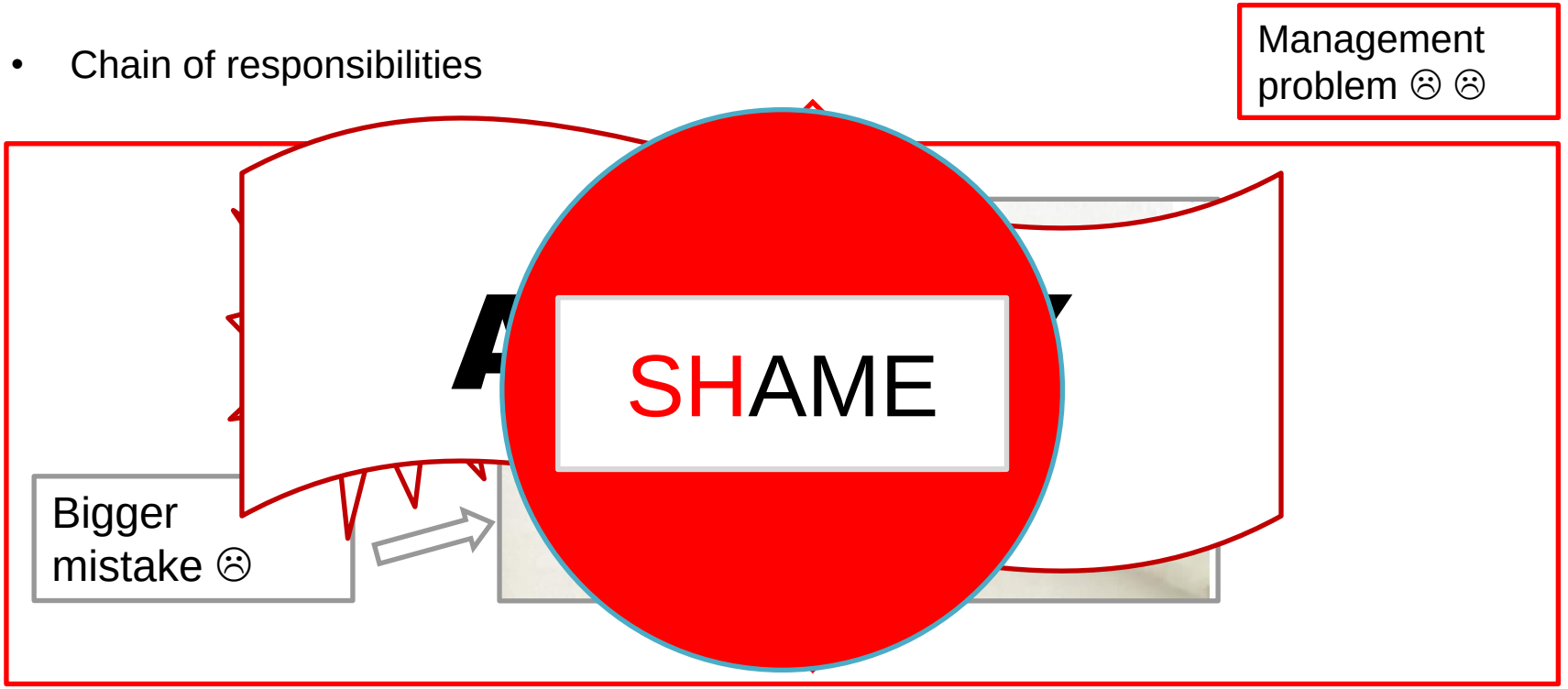
Difficulty of multi-tasking

- Can the analyst always, at every step, anticipate, act, understand AND document everything SIMULTANEOUSLY ?





- Chain of responsibilities

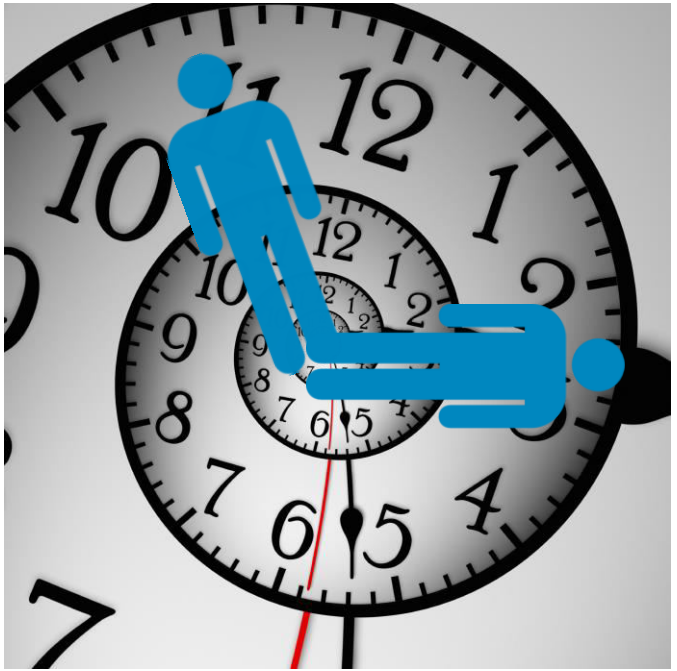


- The pharmaceutical market challenges
- A few drawbacks of “non-automation”
- **Automation principles**
- Automation benefits

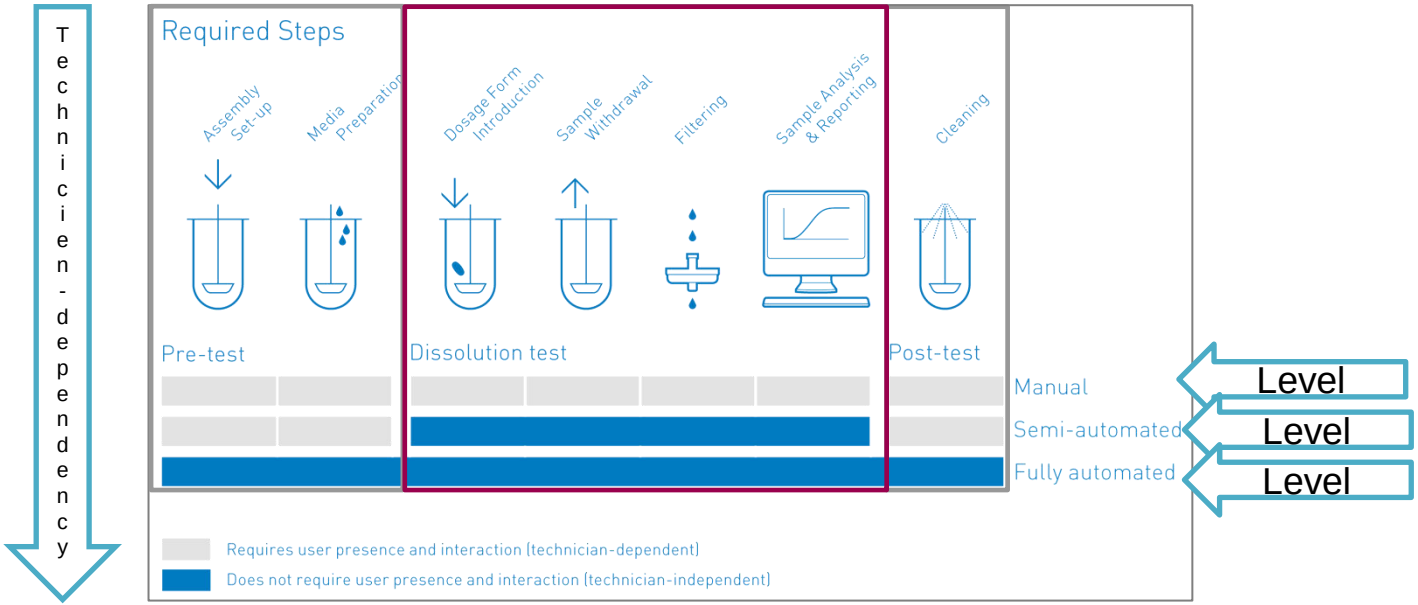
When do technicians lose time?

- Is it overall linear?
- No stress effect ?
- What remains to be done at rush hour?
- Test is the competition, rest is preparation and analysis

Preparing the ROI



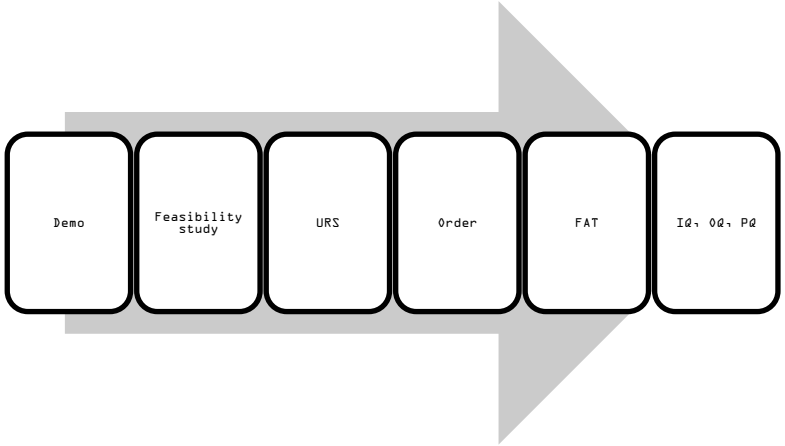
Segmenting the Dissolution process

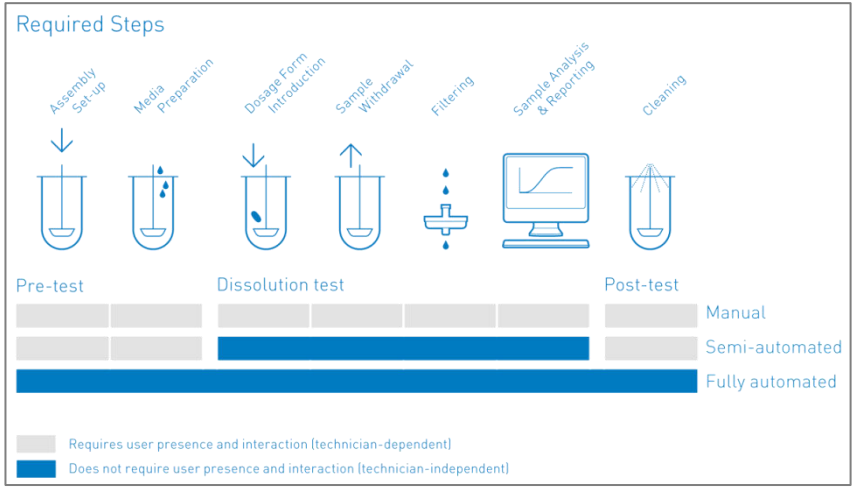


Defining milestones

Cutting the whole implementation process

- Risk is segregated
- Correlates with multiple signatures requirement
- Favors projection and planification





Mastering automation

- Detecting potential artefacts
- Avoiding technology per se
- Automating with priorities
- Easy methods or complicated methods first?
- Outsourcing method transfer?
- Automation should brings extra features/parameters which are MEANINGFUL

Understanding automation

AUTOMATION
4.1 Medium Preparation
4.2 Sample Introduction and Timing
4.3 Sampling and Filtration
4.4 Cleaning
4.5 Operating Software and Computation of Results
4.6 Common Deviations from the Compendia Procedures That May Require Validation

4. AUTOMATION
Automated dissolution systems may be configured in various ways and degrees. The elements of test preparation, initiation, sampling and timing, and cleaning all can be automated. Fully automated systems are available, as are systems where individual steps, such as media preparation or sampling, are automated. This section will discuss operational steps that can be automated.

Should you have any questions or comments, please contact Will Brown, Senior Scientific Liaison, at (301-816-8380 or web@usp.org).

Implementing a strategy: Dosage form characteristics

- How many APIs?
- Dosage
- Release speed
- Stability of dosage form
- Interface solid/liquid
- Handling
- Positioning
- Cleaning

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Implementing a strategy: Method dependent

Method development remains the key

- The method anticipates the scale-up
- It has to be discriminant, robust, informative
- Specification driven (corrective action)
- Automation shall not soften discriminancy

Implementing a strategy: Method duration

ROI are based on the type/duration of Methods

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

13 May 2016
EMA/332805/2016
Committee for Medicinal Products for Human use (CHMP)
Committee for Medicinal Products for Veterinary use (CVMP)
Quality Working Party (QWP)

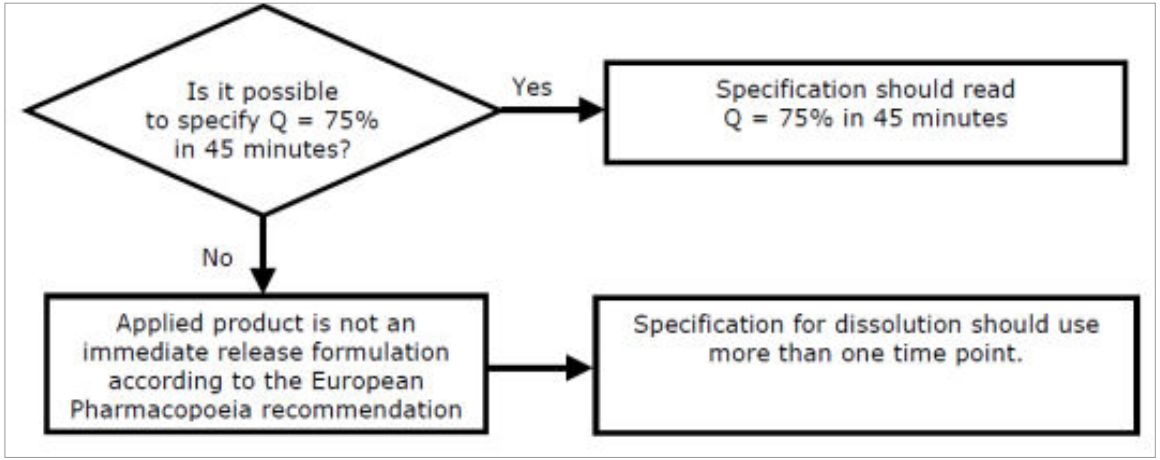
Reflection paper on the dissolution specification for generic oral immediate release products

Draft

Draft agreed by the QWP	March 2016
Draft adopted by the CHMP for release for consultation	March 2016
Draft adopted by the CVMP for release for consultation	April 2016
Start of public consultation	13 May 2016
End of consultation (deadline for comments)	13 August 2016

Comments should be provided using this template. The completed comments form should be sent to QWP@ema.europa.eu

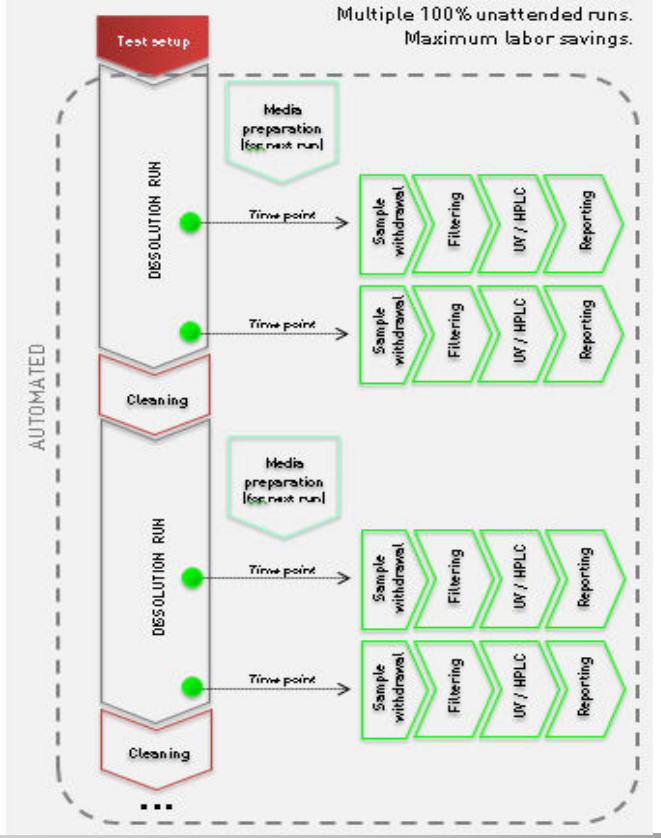
Keywords	Dissolution specification, Generic, Oral immediate release product



Understanding unattended processes

Optimize inter-test savings

- Inter test time is minimized due to multi tasking
- Tasks perceived as tedious are eliminated
- Users can move to other tasks: documentation, data analysis
- Preparation is essential, traceability starts with the test
- Handling of assembly parts is also critical



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Data management reinforcement

V1_MM_061016

MHRA
Regulating Medicines and Medical Devices

MHRA GMP Data Integrity Definitions and Guidance for Industry March 2015

Introduction:

Data integrity is fundamental in a pharmaceutical quality system which ensures that medicines are of the required quality. This document provides MHRA guidance on GMP data integrity expectations for the pharmaceutical industry. This guidance is intended to complement existing EU GMP relating to active substances and dosage forms, and should be read in conjunction with national medicines

Data Integrity and Compliance With CGMP
Guidance for Industry

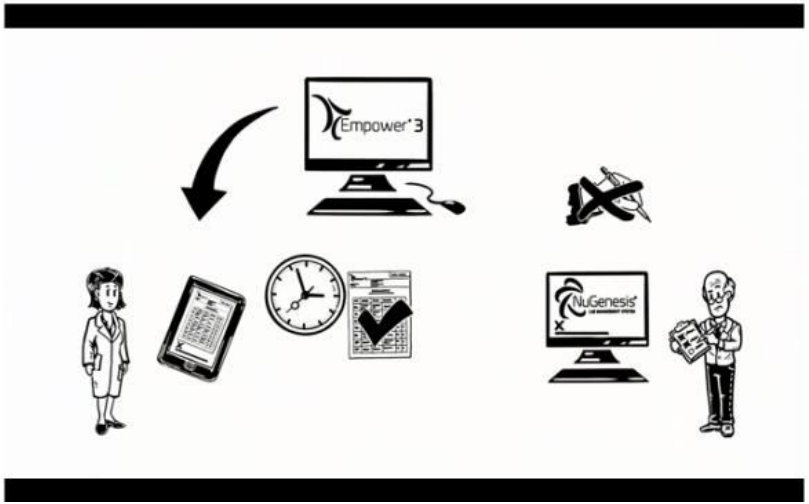
21 CFR part 11

Attributable, **L**egible, **C**ontemporaneous, **O**riginal, **A**ccurate, complete, consistent, enduring, available

Traceability: Data handling

What is your department/company goal?

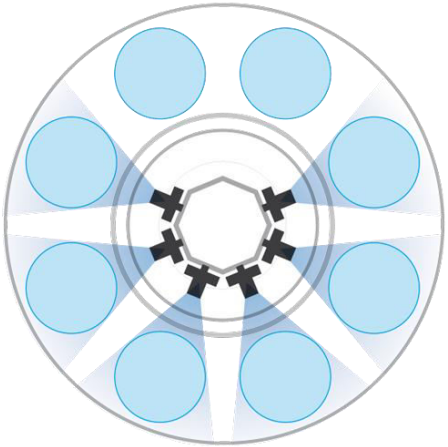
- Quality
- Clarity
- Transparency
- Library
- Support (for other locations)
- Customer or Supplier ?
- Who is the reader?
- Protection of know-how



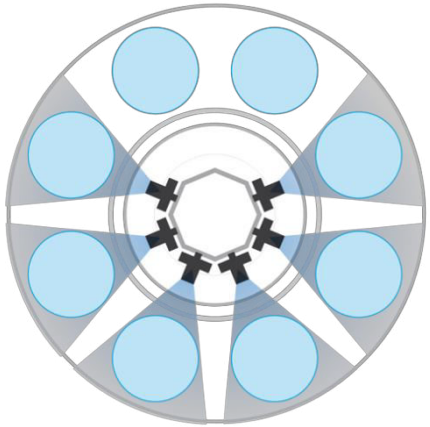
Monitoring or traceability

Experience info or data integrity?

- Video monitoring
- Critical parameters…
- What do we want to know ?
- To see?
- To record?
- Scrutinized or **unattended?**



Unattended doesn't mean unrecorded



2.4.2 OBSERVATIONS

Visual observations and recordings of product dissolution and disintegration behavior are useful because dissolution and disintegration patterns can be indicative of variables in the formulation or manufacturing process. For visual observation, proper lighting (with appropriate consideration of photo-degradation) of the vessel contents and clear visibility in the bath are essential. Documenting observations by drawing sketches and taking photographs or videos can be instructive and helpful for those who are not able to observe the real-time dissolution test. Observations are especially useful during method development and formulation optimization. It is important to record observations of all six vessels to determine if the observation is seen in all six vessels, or just a few. If the test is performed to assist with formulation development, provide any unique observations to the formulator. Examples of typical observations include, but are not limited to, the following:

TRACEABILITY: that also includes Qualification processes !

- The pharmaceutical market challenges
- A few drawbacks of “non-automation”
- Automation principles
- **Automation benefits**

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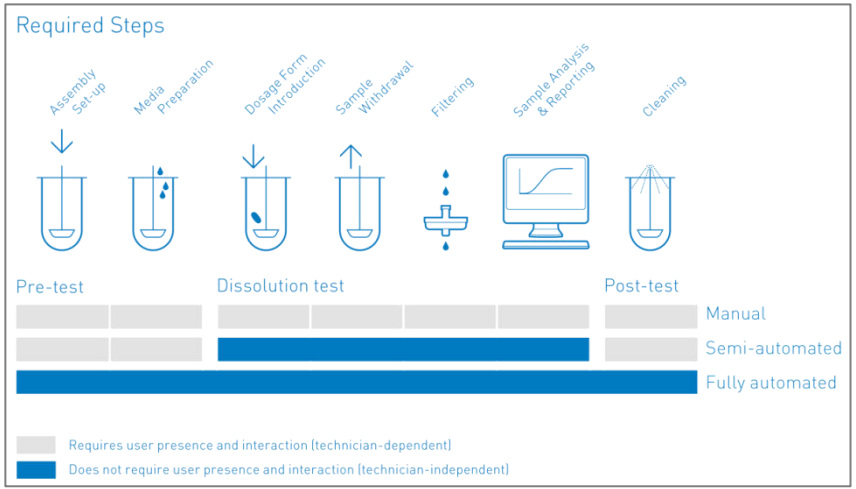
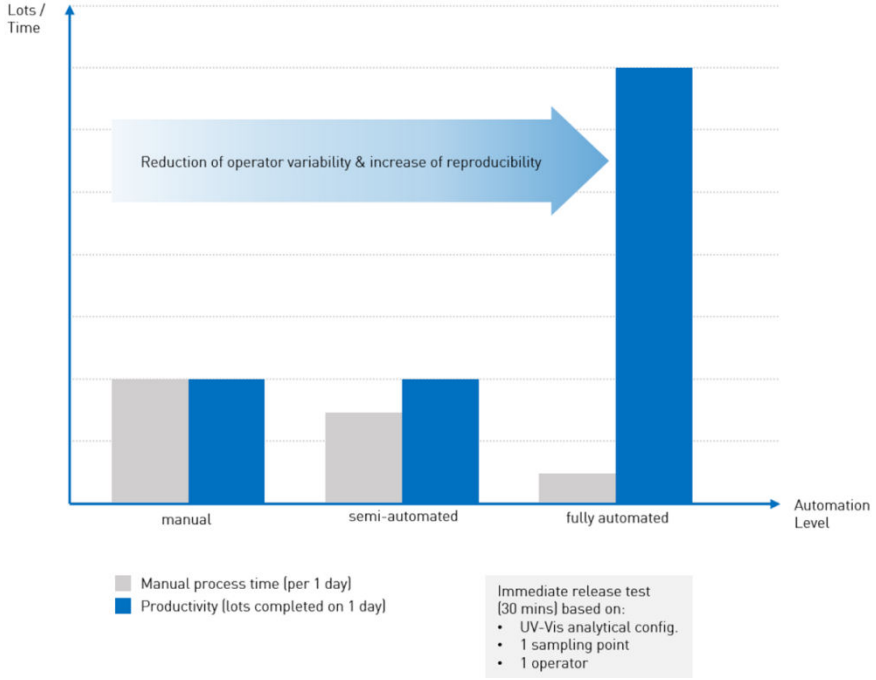
Automation benefit: Reproducibility

Test after test after test…



Automation benefit: Productivity

More batches (increases with IR products)



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Automation benefit: Safety

Qualitative changes

Although difficult to quantify and therefore not usually included in traditional ROI calculations, qualitative changes can be as, if not more important in evaluating the benefit of an automated system. They can impact the achievement of organizational goals. The qualitative change factors evaluated using this method are:

- Quality: *Improved end product quality. The "product" may be data, a purified compound, a cell culture, etc.*
- Safety: *Isolating people from hazards or isolating the process from hazards or contamination.*
- Procedure Enhancement: *A resulting end product with attributes that exceed what was produced or possible to produce manually. This could include such examples as: 1) Increased density or resolution of data; 2) Evaluation of more experimental parameters; 3) Conducting a process is is manually impractical, such as creating high-density microarrays.*
- Audit trail: *A permanent, computer-generated detailed record of process events and results.*
- More timely decisions: *Improved availability or interpretability of process results leading to quicker decisions.*
- Flexibility: *The retention of manipulative skills (in the automation) across staff changes and across labs. The ability to rotate through processes/procedures with no manipulative relearning.*

From Steven D.Hamilton, Hamilton Consulting group

Automation benefit: Adding value to users work

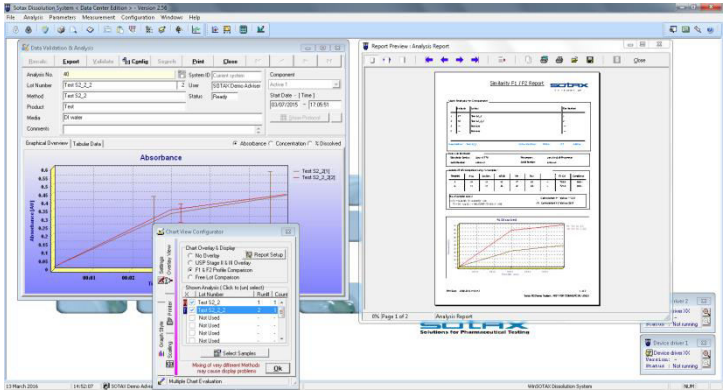
Adding value (quality and technicity) to a job does protect it!

- Cheaper has a limit, what will be next?
- Automation business is also creating jobs
- The whole lab/factory/company is or will be connected and will therefore be pulled to automation
- Software calls for automation

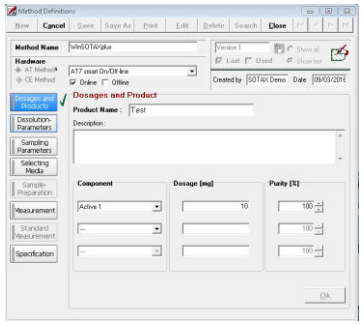
Automation benefit: integration

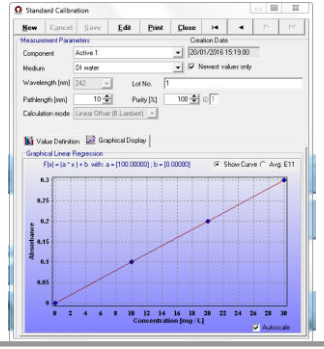
Double on-line

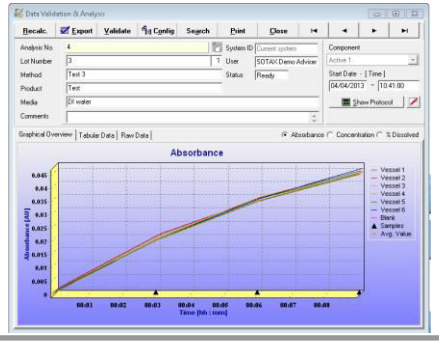
- Results on the fly!
- Double cell changer: 12 results
- F2 comparison by software

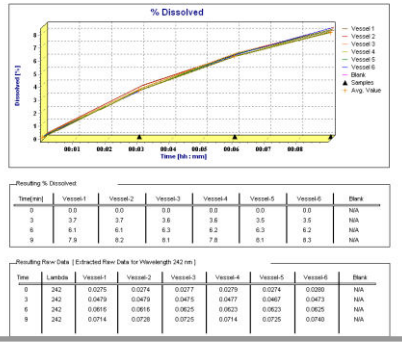


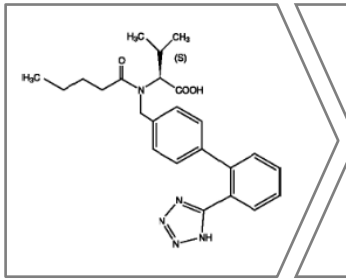
Automation benefit: Integration
Dissolution software: integrated control, calculation, report



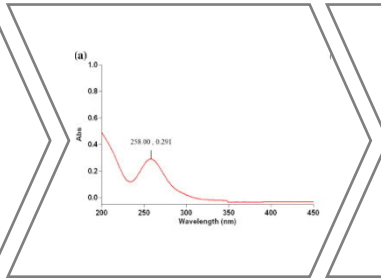




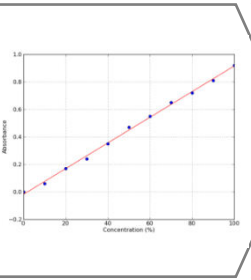




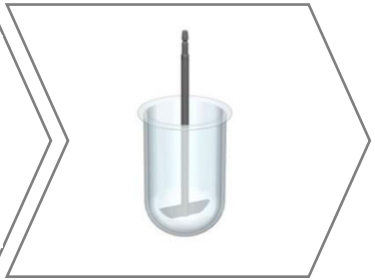
API (molecule)



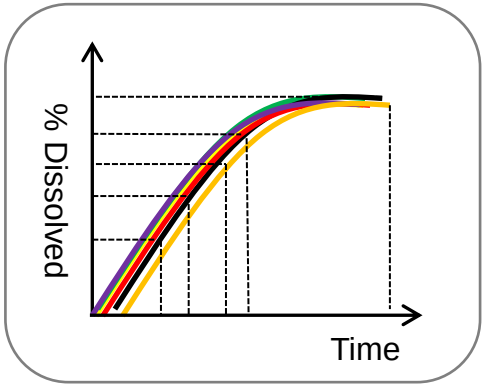
Absorption spectra of API (molecule)



Calibration curve



Dissolution volume



Automation benefit: comparison with manufacturing

QC checks Manufacturing Reproducibility…

Give me 6 tablets, I tell you how good you are ;-)

I made 600 while you asked…:-0)

Automation benefit: comparison with manufacturing

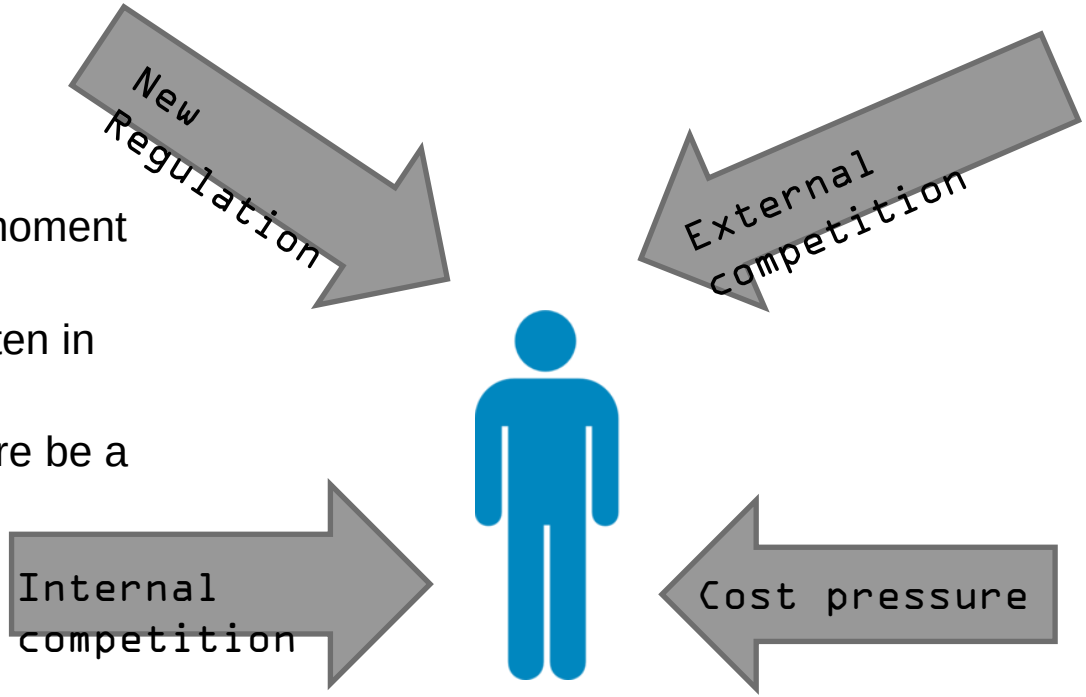
QC checks Manufacturing Reproducibility…

I am checking your blockbuster night and day ☺

I wish I had wheels too…

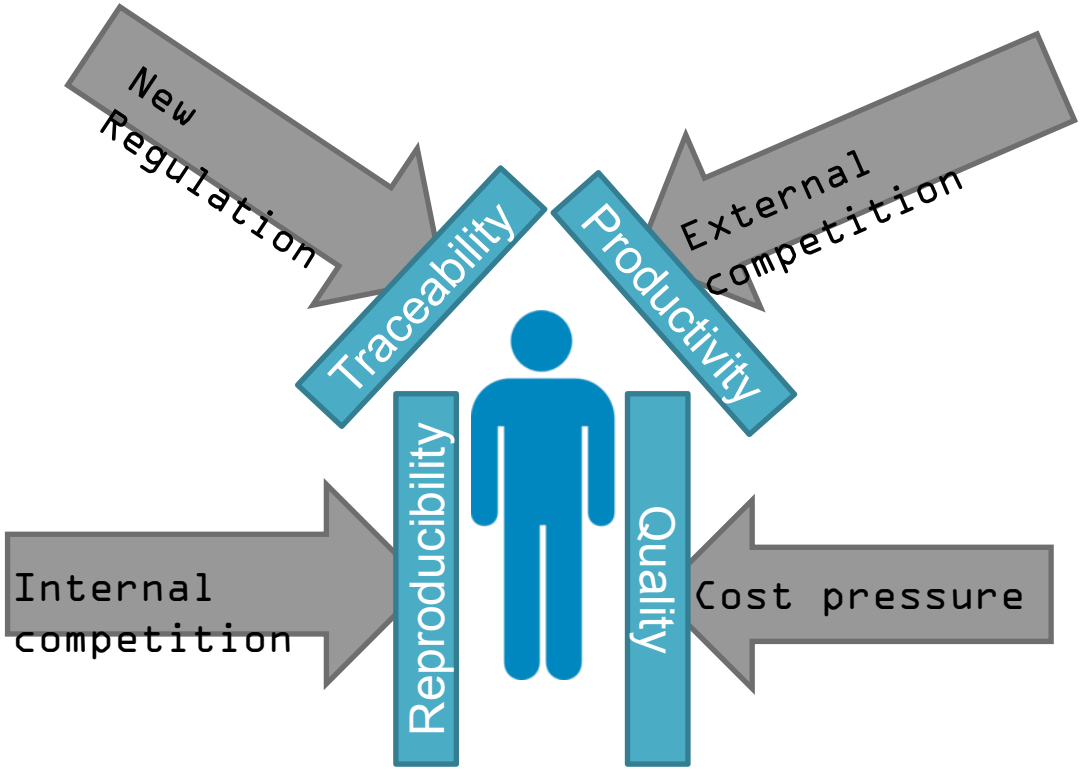
The company context

- In every process or job, there is moment of **evaluation**
- More, faster, better, cheaper is often in the conclusion
- Increasing efficiency shall therefore be a **planned** on-going process



How to increase efficiency

- Improving traceability
- Improving productivity
- Improving reproducibility
- Improving quality



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Conclusion

- **Automated systems add more value to users jobs**. The big pressure on jobs is elsewhere
- Tedious manual processes can always be done elsewhere at a lower price…**so what's next?**
- **Understanding** manual / automation is required for scale-ups and method transfers
- **Anticipating and leading** is always better than accepting
- **Quality , reproducibility and traceability** are mandatory in the pharmaceutical market