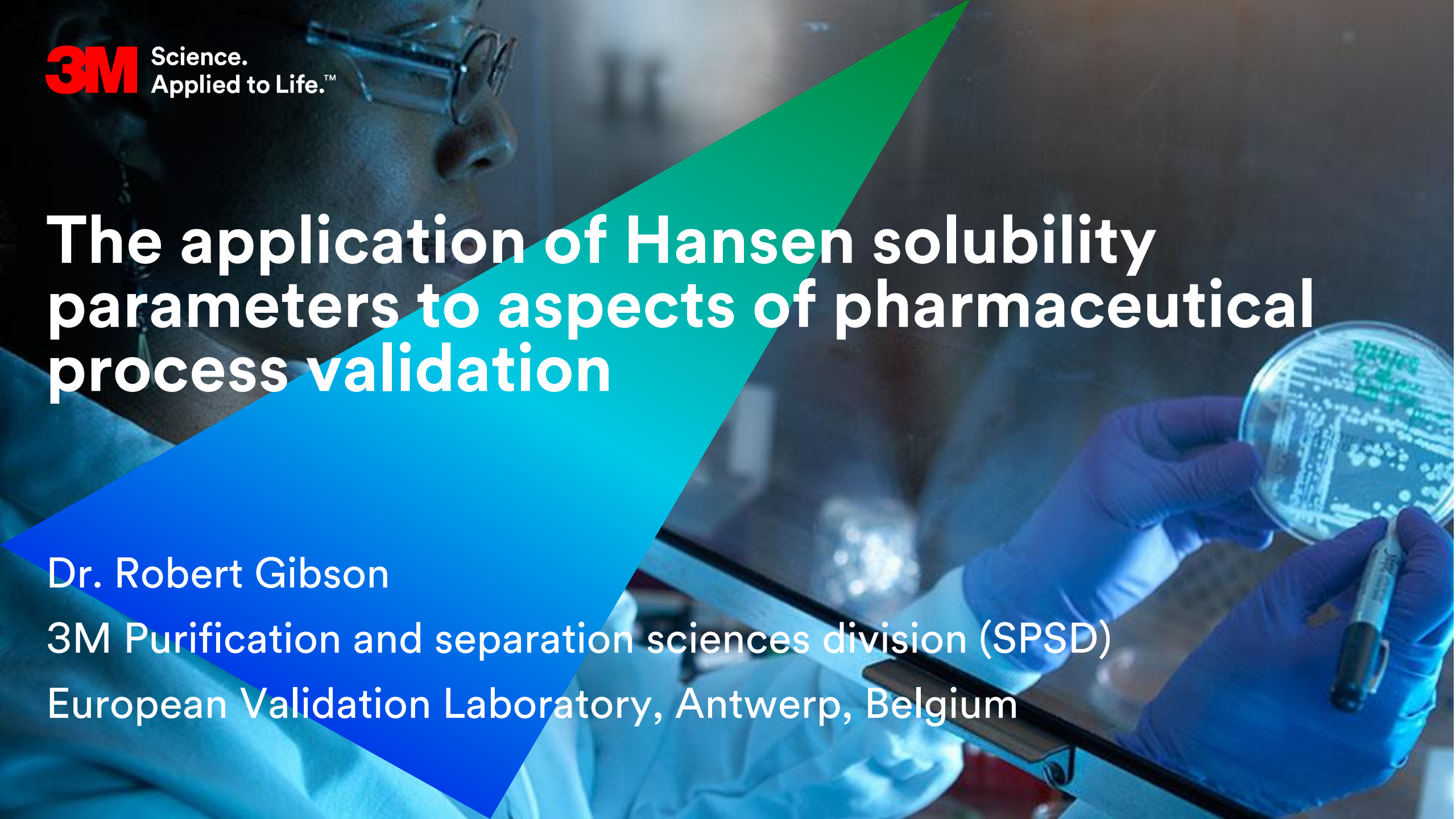


3M Science. Applied to Life.™

The application of Hansen solubility parameters to aspects of pharmaceutical process validation

Dr. Robert Gibson

3M Purification and separation sciences division (SPSD)

European Validation Laboratory, Antwerp, Belgium

3M Science. Applied to Life.™

Introduction

3M produces filtration devices for pharmaceutical customers

Purpose of the filter is to remove particles, aggregates and microbiota

Removal of microbes is critical for product sterility

This must be proven before drug product manufacture

The filter must be “validated”

3M Science. Applied to Life.™

21 CFR 211.91(a) "*not reactive, additive or absorptive to alter safety, identity, strength, quality or purity*"

GMP regulations and every manufacturer must comply

Our focus is on 'reactive' and 'additive'

3M Science. Applied to Life.™

Process validation:

'the collection and evaluation of data, from the process design stage through the commercial production'

'establishes evidence that a process is capable of consistently delivering quality product'

Process design > process qualification > process verification

FDA guidance for industry on process validation

3M Science. Applied to Life.™

Single-use systems (SUS) are rapidly becoming used throughout the pharmaceutical industry

In biopharma, an increase of >10 % CAGR is expected with a multi billion dollar market size in 2019

One hurdle often cited to implementing SUS is compatibility of materials and Extractable and Leachable testing

3M Science. Applied to Life.™

Single use filtration media

Used throughout aseptic processing steps

Composed of plastic material

Typically, exposed to large volumes of drug products (>1000 litres)

Membrane contains a large surface area

High potential for interaction between solvent/media and polymeric materials

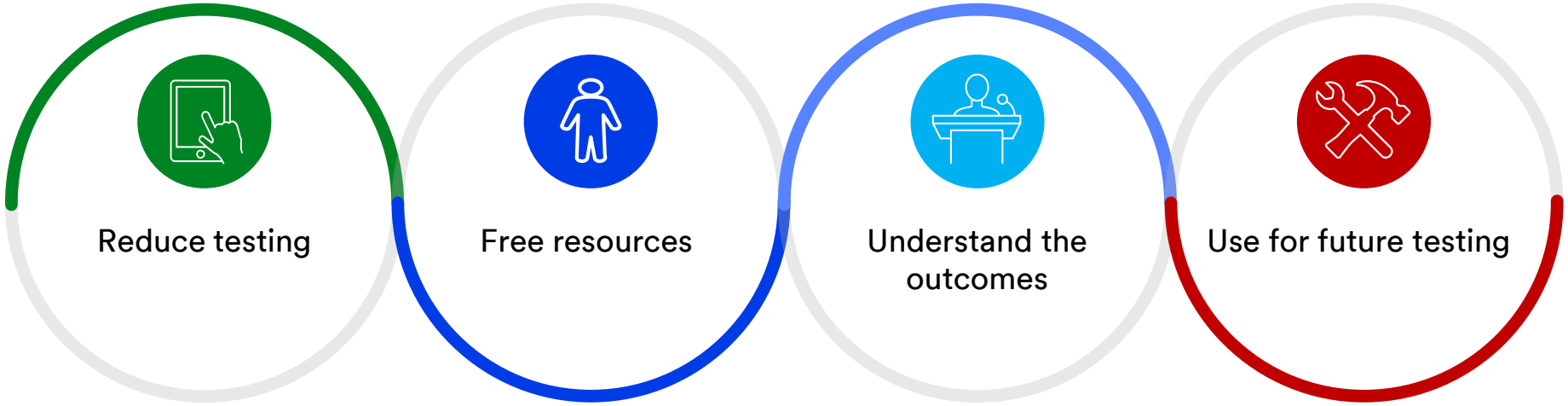
3M Science. Applied to Life.™

The problem

Component	P_1	P_2	P_3	P_4	P_5
Component 1	2	0.5	14	23	20
Component 2	1	0.5	6.5	6.5	10
Component 3	-	20	3.4	5.8	0.9
Component 4	51	35	25	45	51
Component 5	-	4	36	19	8
Component 6	46	40	15	-	10
Component 7	-	-	0.1	0.7	0.1
Density min					1.2
Density max					1.7
pH min	8.5	8.5	8.5	8.5	8.5
pH max	9	9	9	9	9

3M Science. Applied to Life.™

“Imagine if we could….”

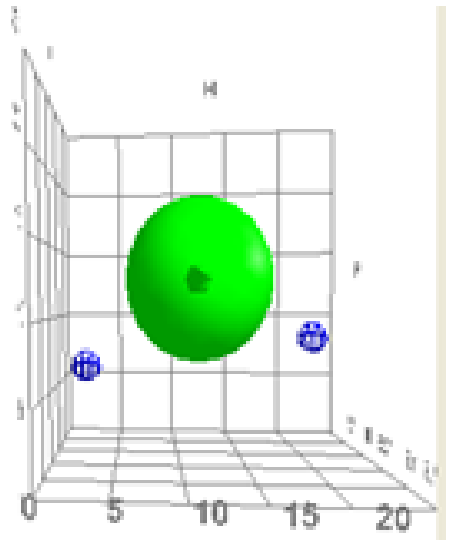


01 Streamline testing procedures

02 Allow people and instruments freedom to work on high value tasks

03 Why did my test fail? Chemical compatibility or incorrect process conditions

04 Speed up future testing, reduce costs etc



Solubility sphere showed triggered some interest

Not interested in solubility

Need to know when a polymer/solvent pair will ***not*** dissolve

Determine the ‘extremes’ of compatibility: when or when not to test

Next step to develop a performance test to compare compatibility

Development of a performance test

Compatibility testing

Performance test

- Diffusion test is used throughout filtration applications
- Measurement of air through liquid contained in pore spaces of filter
- Correlated to the ability of the filter to retain bacteria

01 Pre-filtration test

02 Process simulation
8 hours, room temperature

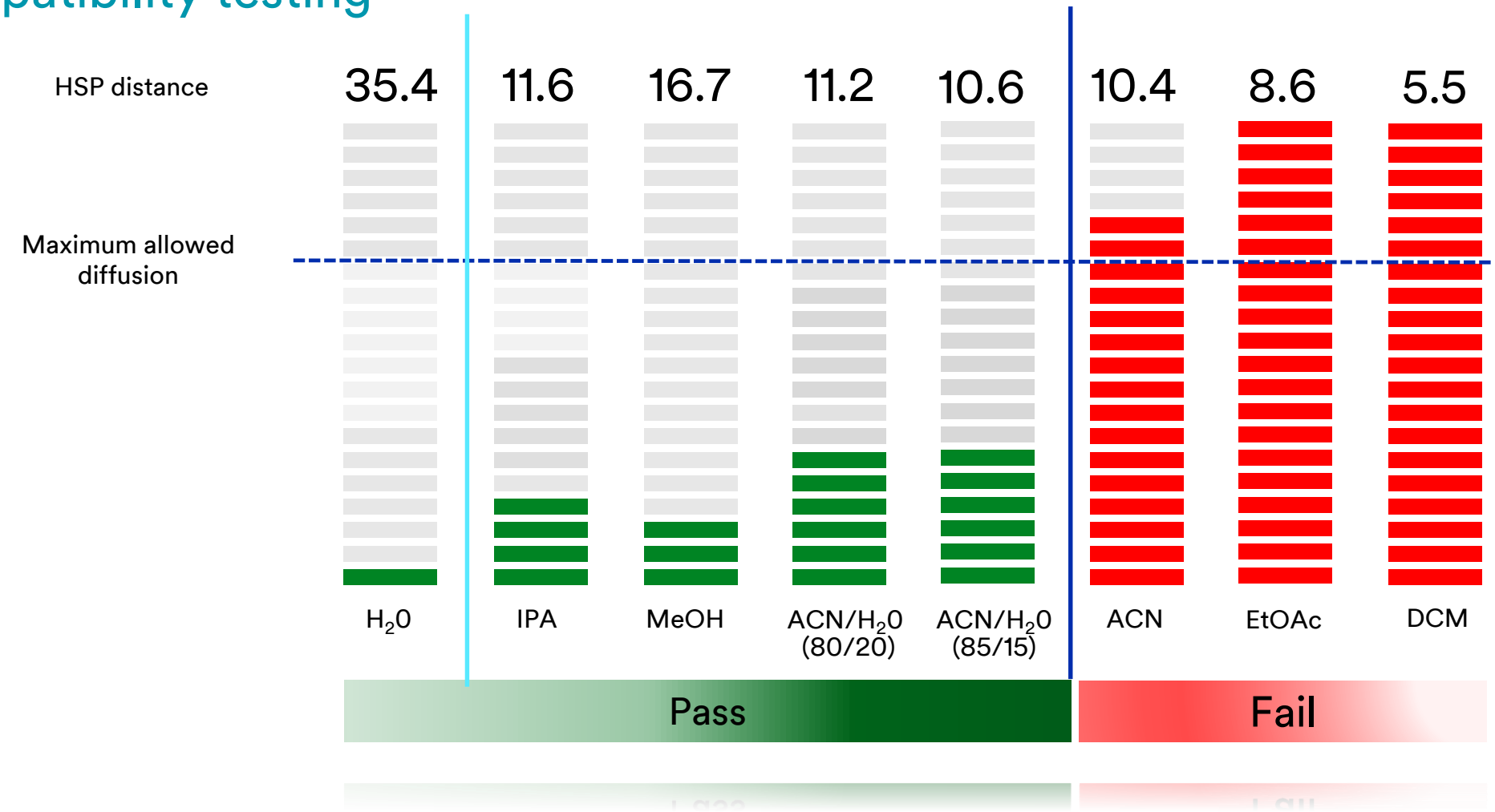
03 Product removal

04 Post-filtration diffusion test
Results categorized into three; Pass, fail and difference > 10%

05 Compare tests with HSP distances
Determine HSP limit for our filter

Results

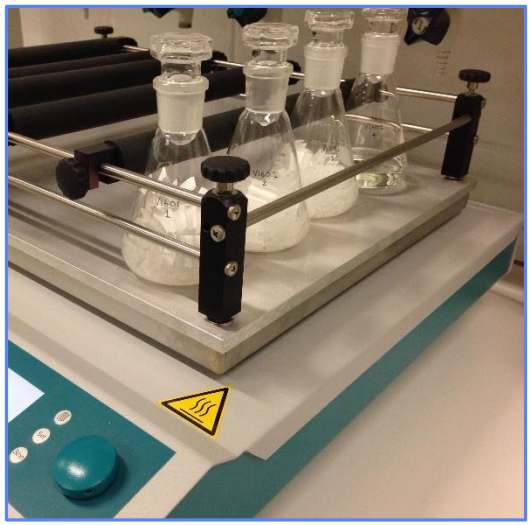
Compatibility testing



This method allows us to determine if a filter will be compatible with any given solvent with known values of HSP.

Extractable assessments

‘Simulated leachable test’



Worst case w/ respect to time and temperature. Similar to process conditions. Model solvent.

Could we correlate the amount of non-volatile residue to the HSP distance between solvent and polymer?

Polymer is the material of construction, solvent is the extraction solvent

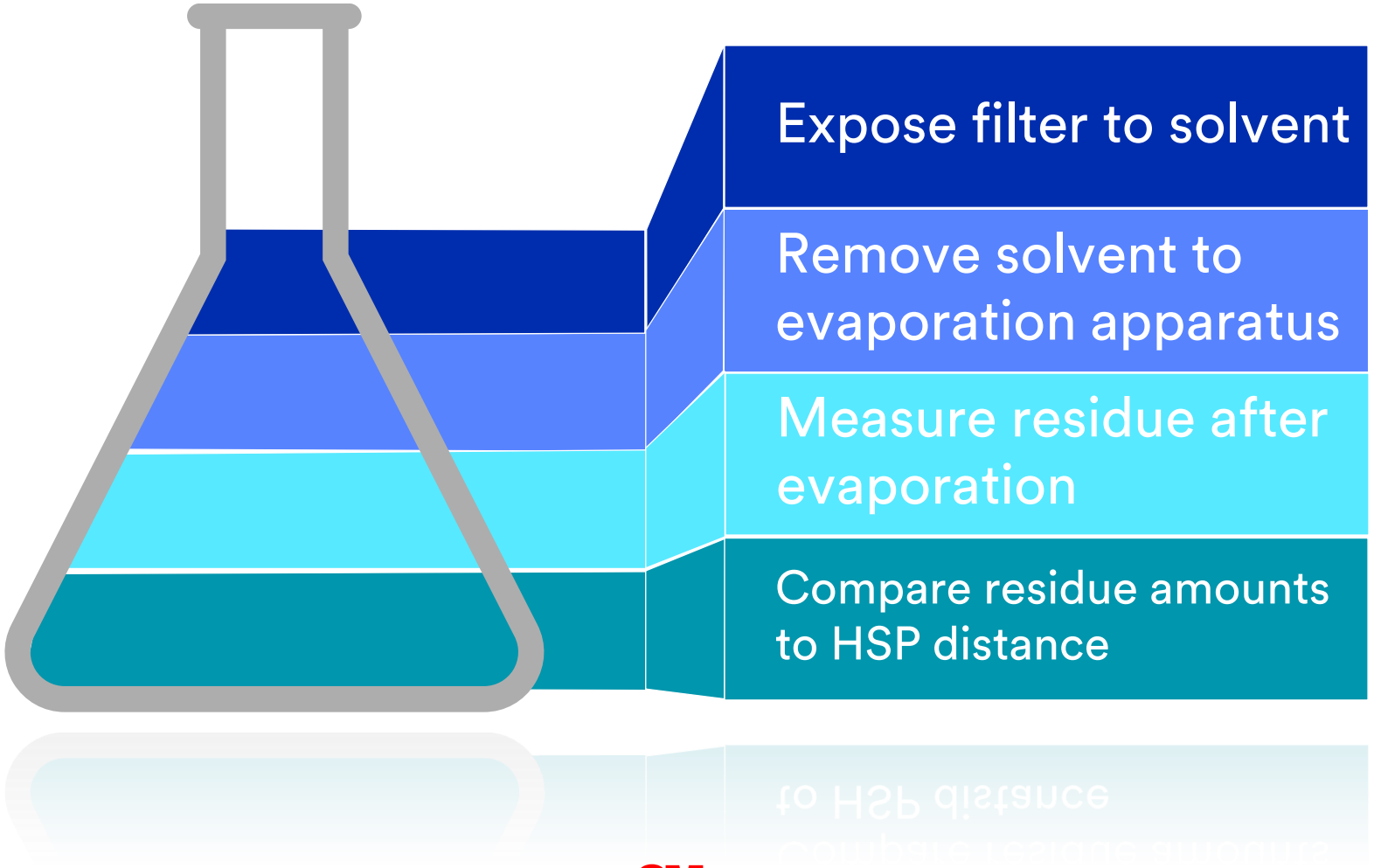
Extraction solvents are often chosen to mimic process fluids

The drug product will contain many non-volatile components

“Out-dated” test that is still employed by many manufacturers

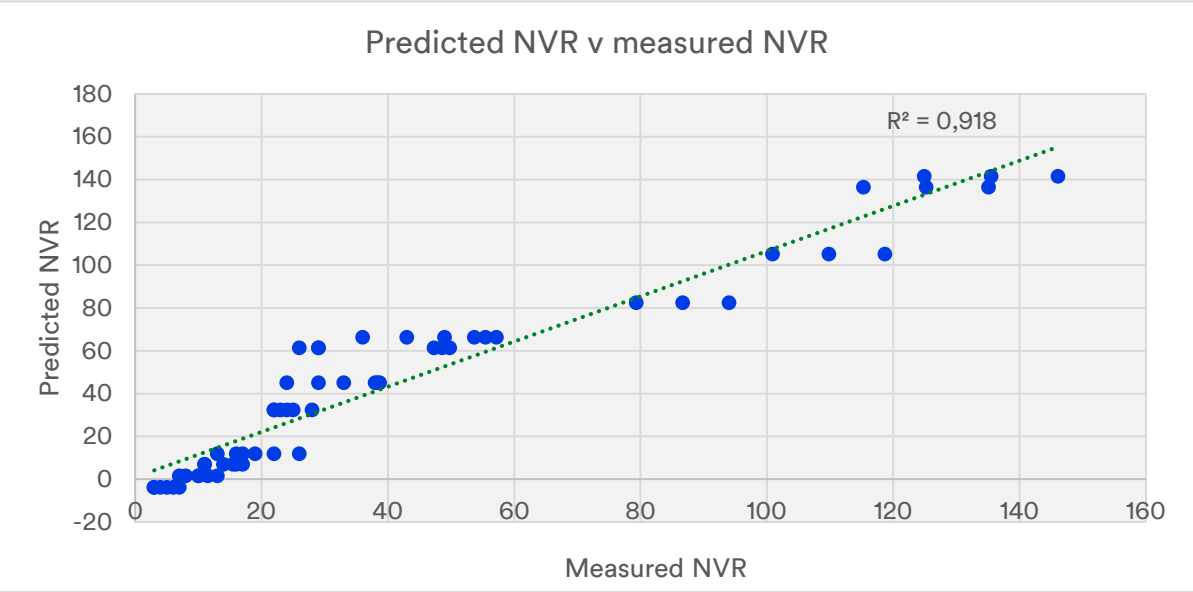
Extractable assessments

Procedure



Summary of testing

Amount of NVR at time X for a solvent/filter combination can be calculated



Predicted vs actual values for extractions of membrane in four solvents

Solvent	Predicted	Actual
Isopropanol	11	14
Propylene glycol	6	2
Ethyl Acetate	27	26
Heptane	55	52

All data: results from 89 extractions (1 - 72 hours)

Reduce lab time, costs, resources

Applications to pharma market and beyond

Conclusions

Our data show the benefit of applying HSP to understanding compatibility testing

Allows an upfront assessment of NVR testing

Reduces testing time, removes the need to resource experiment

Important tool in the first steps of material selection for process development

Future work