

Colour Management For Formulators

23rd October 2013

Colours in Pharmaceutical Products

Marcel Cimpan

Senior Manager Customer and Technical Services



Agenda

- Uses for colours in the Pharmaceutical industry
 - Colorcon Brand Enhancement Services
- Pigments available
 - Oxides
 - Lakes
 - Non synthetics
- Global colours
- Regulatory
 - Quantity restrictions
- Film coat formulation
- Colour measurement and control
- Coating application

Uses for colours

- **Colouring of coating systems**
- Colouring of core tablets
- Colouring of liquid and semi-solid products
- Food and confectionery

Why differentiate at the dosage level?

Do you recognize this drug?



- No distinctive shape and color
- No memorable image

- No trademark protection
- No brand equity
- Increased risk of mix up on the production line and therefore potential product recall
- Increased risk of counterfeiting

Lack of branding does not help patient compliance

Disturbing Facts....

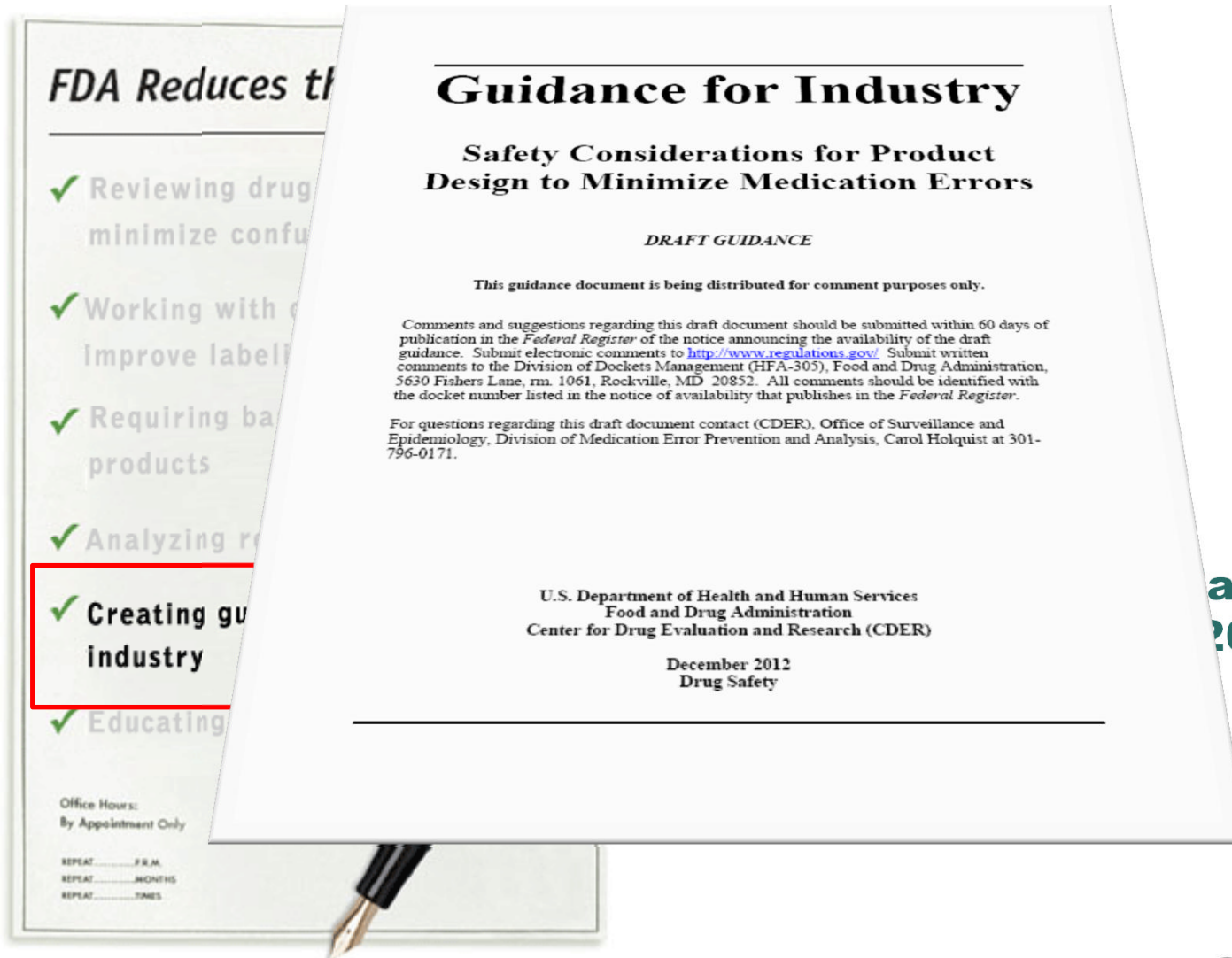
Medication errors cause **7,000 deaths each year** ” ([FDA](#))

At least **1.5 million Americans** are sickened, injured or killed each year **by errors in prescribing, dispensing and taking medications** ([Washington Post](#))

Treating the related injuries **cost an estimated \$3.5 billion a year** ([Washington Post](#))



FDA Concern



ance
2012

FDA Draft Guidance

Different strengths – same look -
potential overdose






There is a need to differentiate

- Patients are consumers
- Studies have proven that consumers form an emotional link with colour*
- Examples of drugs where GERX manufacturer used unique shape/color and got higher counting unit sales than others are in the following slides

* (ref: Some aesthetic considerations for over-the-counter (OTC) pharmaceutical products; International Journal of Biotechnology, Volume 11, 2010)

“Branded” Generics with higher market shares than plain, white tablets



Therapy	Generic name/API	Tablet image	Manufacturer	Coated or uncoated	2012 CU (000's)
Antipsychotic	Quetiapine 25mg		Teva	Coated	145,656
	Quetiapine 25mg		Lupin	Coated	119,586
	Quetiapine 25mg		Roxane	Uncoated	73,676

* tablets are not to scale so size comparisons should not be made

The information contained in this presentation is proprietary to Colorcon and may not be used or disseminated inappropriately.



“Branded” Generics with higher market shares than plain, white tablets

Therapy	Generic name/API	Tablet image	Manufacturer	Coated or uncoated	2010 CU (000's)	2011 CU (000's)	2012 CU (000's)
Anti-convulsant	Levetiracetam 750 mg		Lupin	Coated	133,394	224,581	219,142
	Levetiracetam 750 mg		Mylan	Coated, white	195,279	185,740	150,016

Interestingly Mylan was the first to file, but after the first year volume dropped to the pigmented Lupin dose

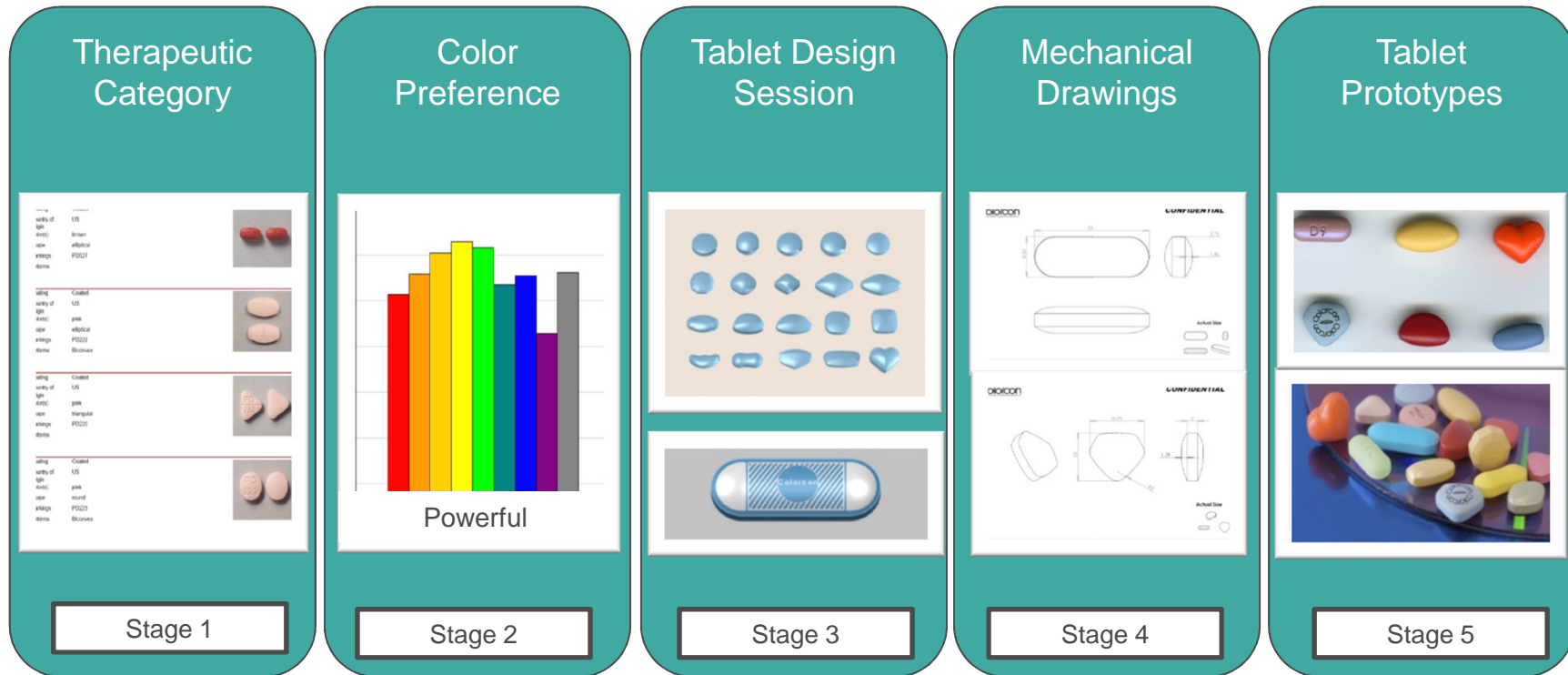
* tablets are not to scale so size comparisons should not be made

The information contained in this presentation is proprietary to Colorcon and may not be used or disseminated inappropriately.



Brand Enhancement Services

Colorcon can help you differentiate:



Improving speed to market from months to weeks

The information contained in this presentation is proprietary to Colorcon and may not be used or disseminated inappropriately.



Pigments used in film coatings

- Metal Oxides
 - Titanium Dioxide
 - Iron Oxide Red
 - Iron Oxide Yellow
 - Iron Oxide Black
- Aluminium Lakes
- Non synthetics

Types of Pigment

Oxides - Titanium and Iron

- good chemical and light stability
- small particle size
- little batch-to-batch colour variation
- low cost
- excellent opacity
- wide regulatory acceptability
- restricted colour range
- rather dull colours

Advantages

Disadvantages

Types of Pigment

Aluminium lakes

- wide range of bright colours
- brightness retained when mixed together
- low opacity compared with other pigments
- colour depends on particle properties - batch variation
- tendency to form gel structure in liquid products
- some colours show poor stability

} **Advantages**

} **Disadvantages**

Types of Pigment

■ Non-synthetic colours

- natural or nature-identical claim
- consumer acceptability?
- low colour strength
- high cost
- residual taste and odour
- restricted colour range
- batch-to-batch color variation
- very poor chemical and light stability

Advantages

Disadvantages

Examples of non synthetic colours

Examples of colours exempted from certification

- Annatto extract
- Dehydrated beets (beet powder)
- Caramel
- [beta]-Apo-8'-carotenal
- [beta]-Carotene
- Cochineal extract; carmine
- Toasted partially defatted cooked cottonseed flour
- Grape color extract

Examples of colours approved for ingested drugs

- Paprika
- Paprika oleoresin
- Mica-based pearlescent pigments
- Riboflavin
- Saffron
- Tomato lycopene extract; tomato lycopene concentrate
- Turmeric
- Turmeric oleoresin

Global Acceptable Pharma Colors

US, EU, Japan

- Only a limited number of colors are acceptable for global (US/EU/JP) use:
 - FD&C Blue # 2 (Indigo Carmine)
 - FD&C Blue # 1 (Brilliant Blue)
 - FD&C Yellow # 6 (Sunset Yellow)
 - Titanium Dioxide
 - Iron Oxide Red
 - Iron Oxide Yellow
 - Iron Oxide Black

Regulatory restrictions - summary

- Country specific
- Main regulatory bodies: FDA (USP, GRAS), EU, JP
- All these will list colorants exempted from certification, approved colorants, approved colourants with quantitative limits, banned colouring agents
- In some cases there will be specific regulations or labelling requirements when used in products for children (age specific, eg EU under 36 month)
- Specific labelling requirements when used in food additives or nutritional products
 - Indigo carmine - JP – max 0.1% by w. of color
 - BOx - JP – max 1.539 mg/day oral
USP – 5mg/day elemental iron
 - ROx - JP – max 95.4 mg/day oral
USP – 5mg/day elemental iron
 - YOx - JP – max 5.67 mg/day oral
USP – 5mg/day elemental iron
 - Sunset yellow - JP – max 0.1% by w. of color

Example:

Japanese regulatory only allows 5.67mg of yellow iron oxide per day.

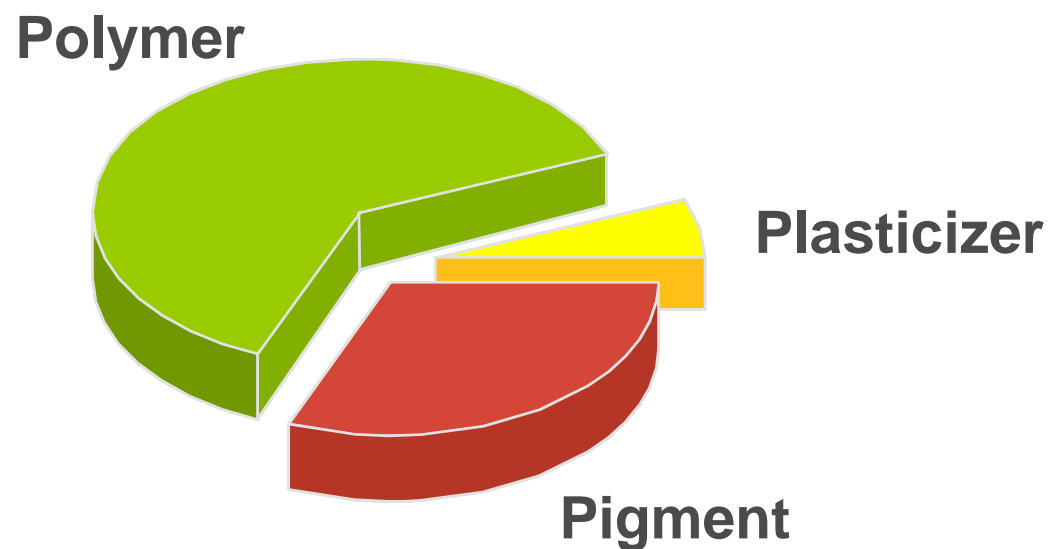
For a 1000mg tablet a 3% weight gain of film is 30mg:

- one tablet a day could therefore contain a maximum of 5.67mg YOx
- four tablets a day is 1.4175mg YOx

Coating formulation

Opadry®
Complete Film Coating System

A pre-dispersed powder containing

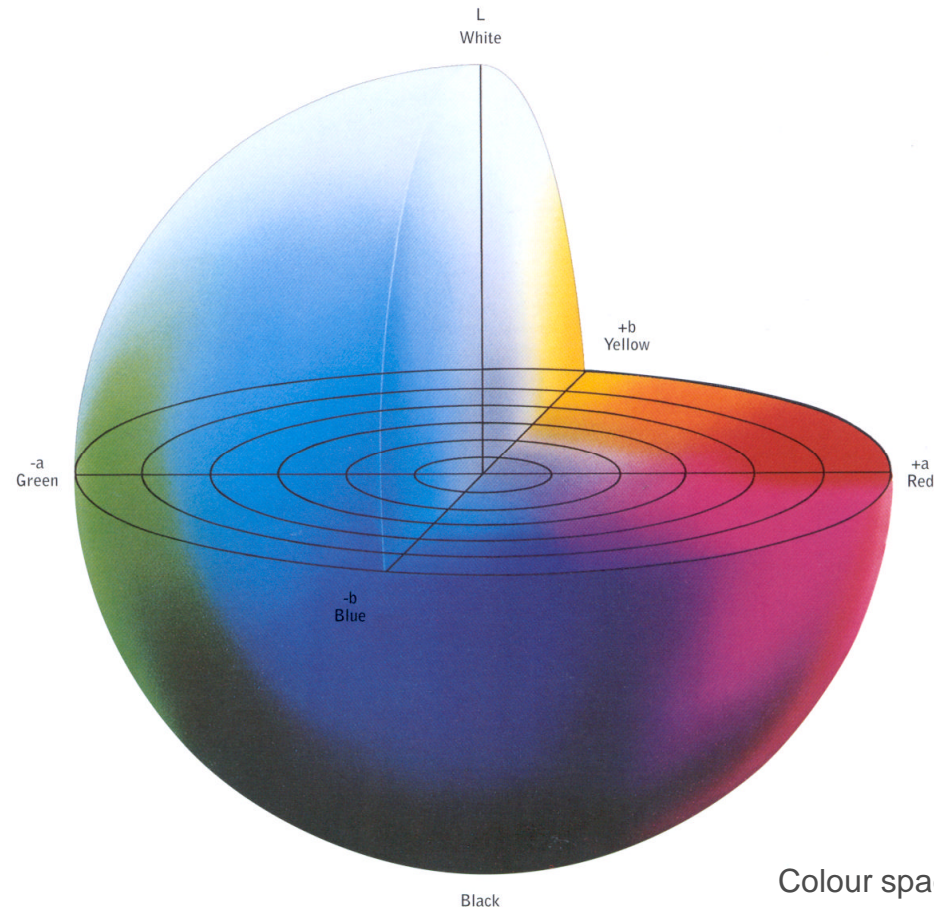


.... in optimal ratios

Colour measurement

- CIELab
- Measurement
- Factors influencing colour

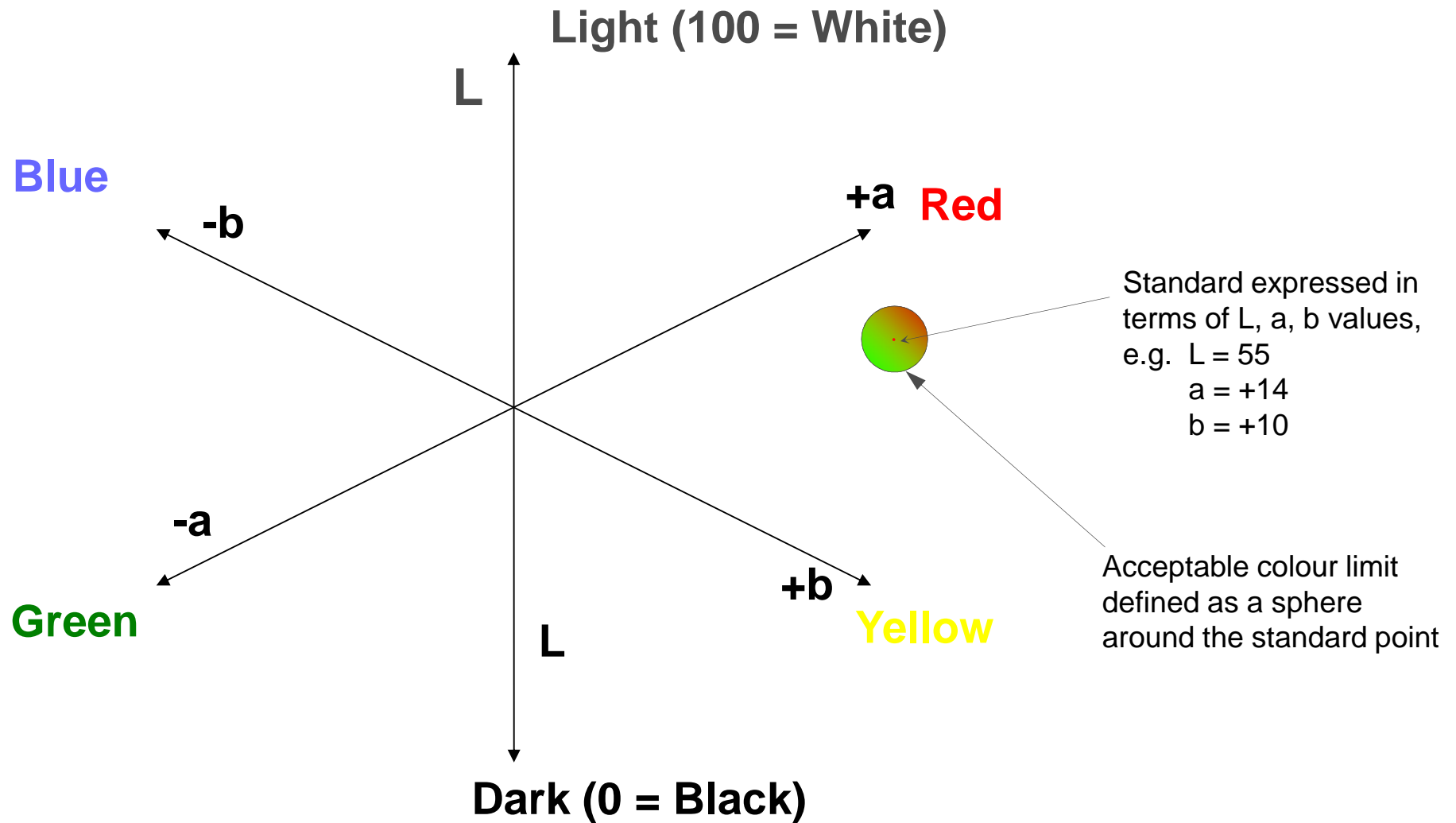
Representation of CIE L*A*B* Colour Space



Colour space diagram courtesy of Datacolor



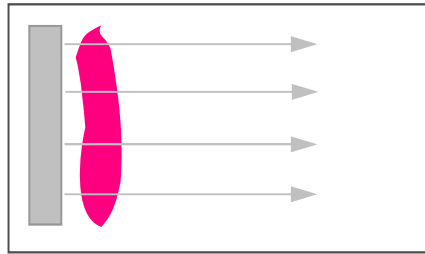
CIE L*A*B* - Colour Space Diagram



Colour Control - Reflectance Spectrophotometry



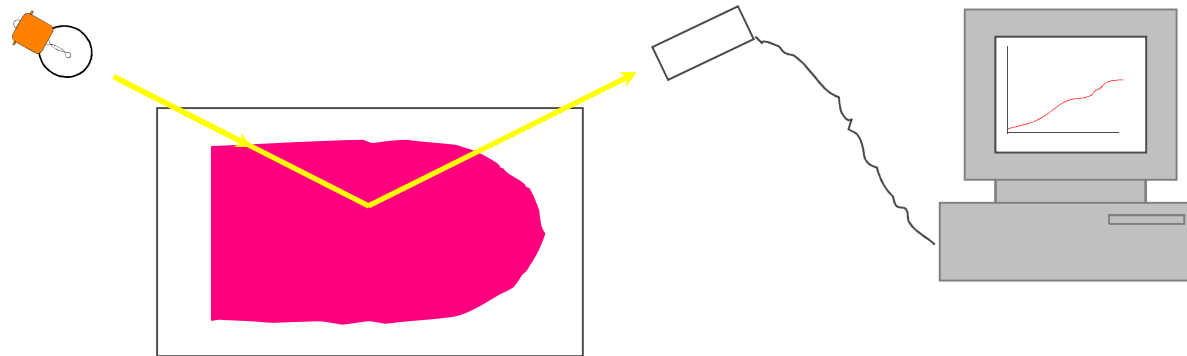
Standard white drawdown card



Liquid dispersion of sample

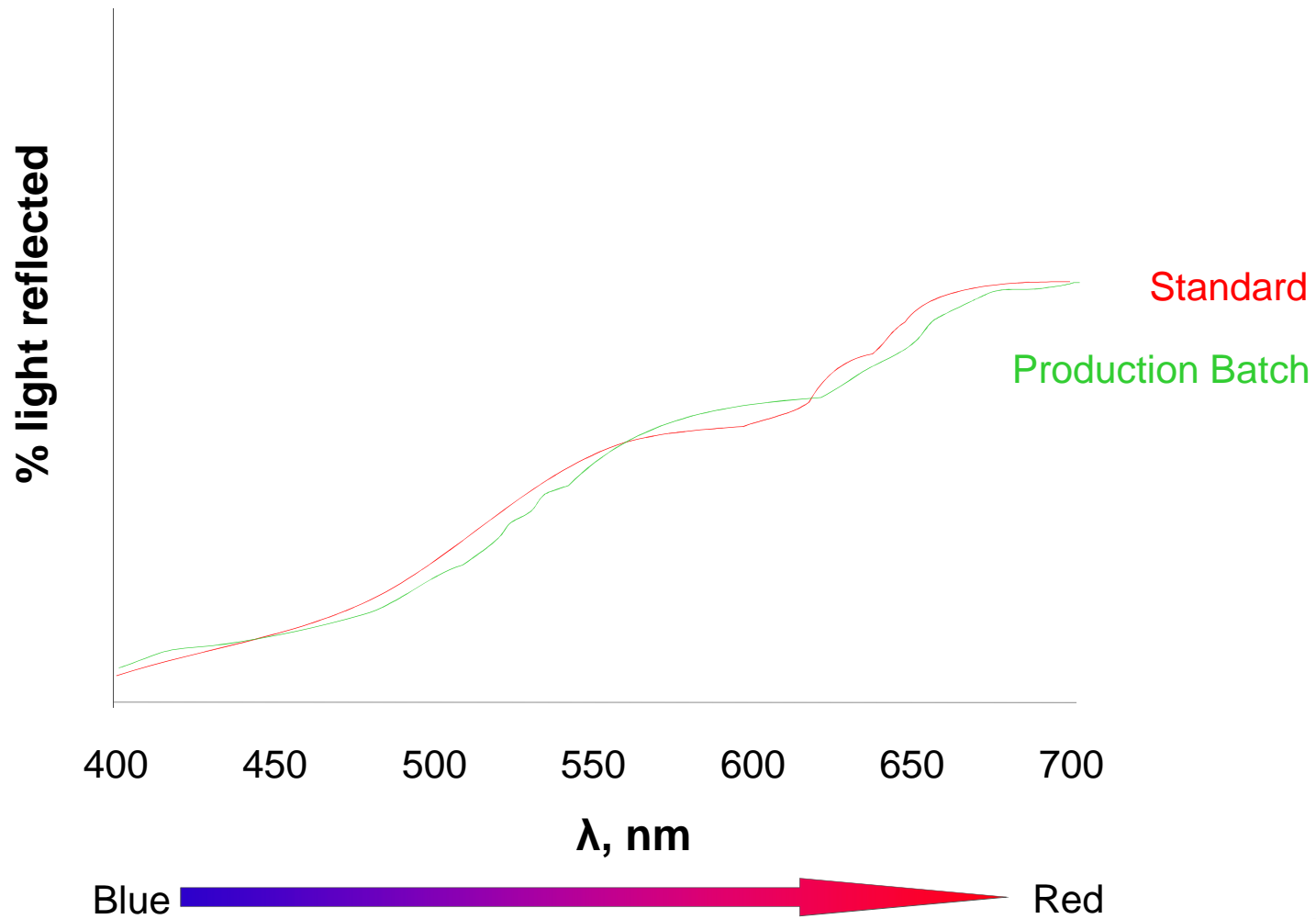


Drawdown using standard thickness bar



Measure quantity of light reflected across the visible spectrum

Colour Control - Reflectance Spectrophotometry



Blue  Red



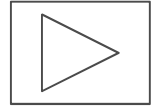
Factors Influencing Colour

- Type of light used (metamerism)
- Colour is subjective:

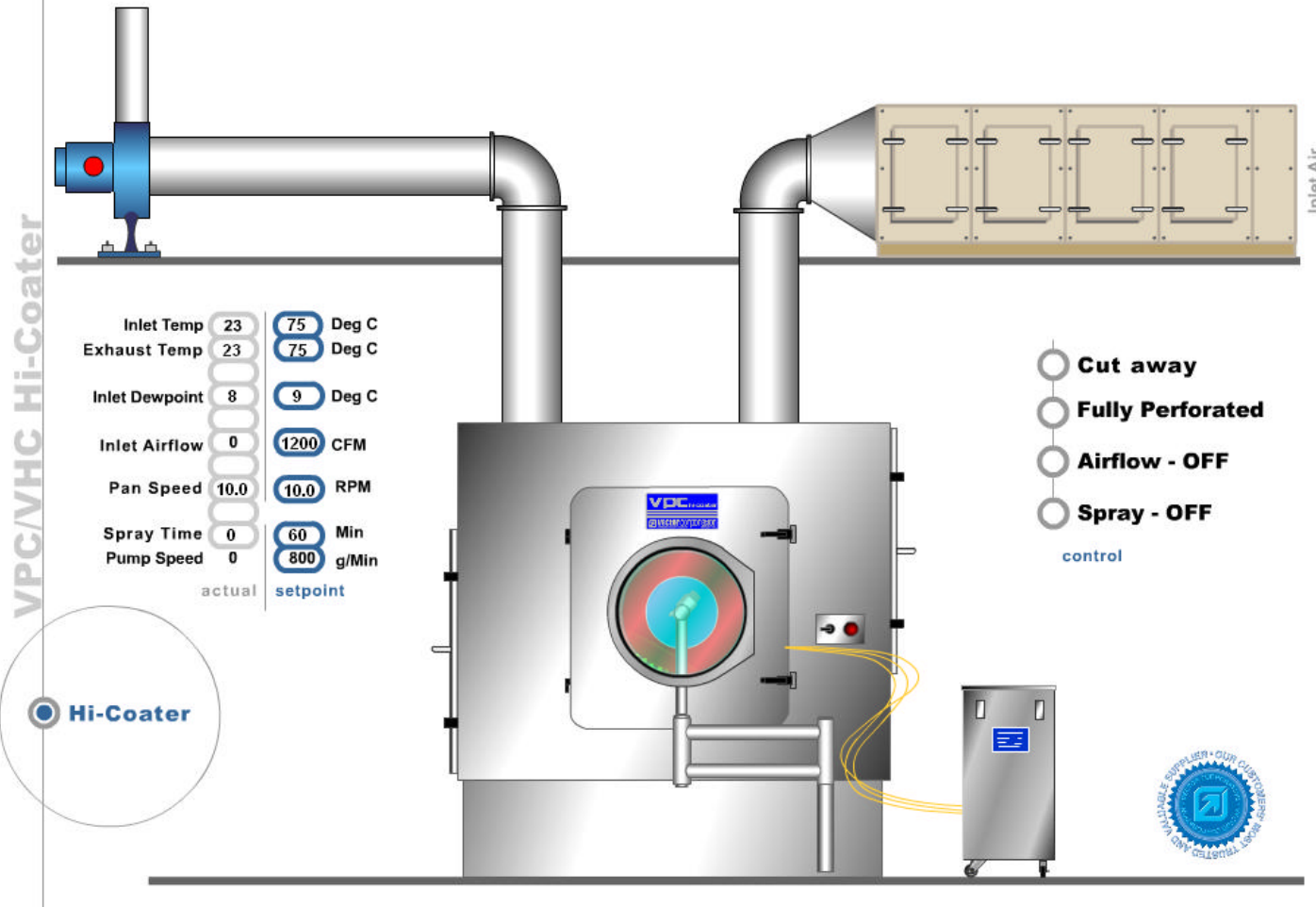
COLOUR IS A SENSATION WHICH ONLY EXISTS INSIDE THE BRAIN

- Tablet shape
- Tablet coating roughness

Coating application



vector corporation
A FREUND GROUP COMPANY



The information contained in this presentation is proprietary to Colorcon and may not be used or disseminated inappropriately.



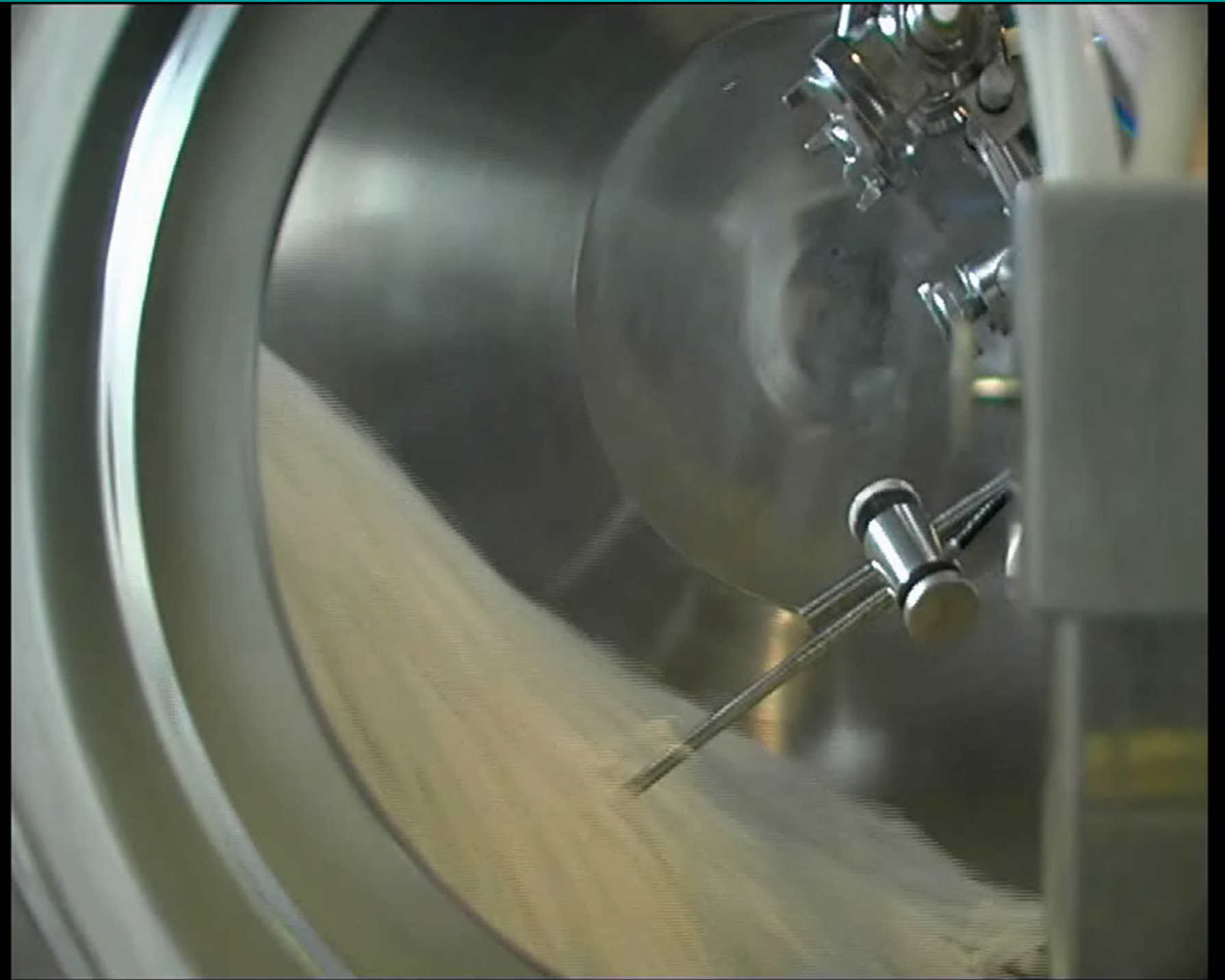
Coating application – spray gun

Manesty ABC



The information contained in this presentation is proprietary to Colorcon and may not be used or disseminated inappropriately.





Coating application – coating system comparison

Evaluation of Tablets

- Color development and uniformity
 - Sampled at 5 minute intervals and compared to the final tablet reference color
 - Target ≤ 1 DE from reference



Coating application – coating system comparison

Final Tablet Appearance



Opadry II PVA



HPMC

Conclusion

- Colours are extremely important in pharmaceutical use.
- There are many controls and limitations on their use.
- Control of batch to batch colour variation is vital.