

USP/PDA Joint Conference: Residual Solvents

Pharmaceutical Manufacturer Perspectives

Tina M. Engel, PhD
The Procter & Gamble Company



P&G

OTC Perspective

Comparison of OTC and Rx drug products

Implementation of USP residual solvent guidelines?

Potential business impact

Discussion points



OTC Drug Categories

Acne
Allergy
Analgesic, External
Analgesic, Internal
Anorectal
Antacid
Anthelmintic
Antibiotic, First Aid
Anticaries
Anticholinergic
Antidiarrheal
Antiemetic
Antiflatulent
Antifungal
Antihistamine
Antimalarial
Antimicrobial
Antiperspirant
Antipyretic
Antirheumatic
Antitussive
Aphrodisiac
Astringent
Benign Prostatic Hypertrophy
Boil Treatment
Bronchodilator
Cholecystokinetic

Cold and Cough
Callus Remover
Corn Remover
Dandruff
Decongestant, Nasal
Dental Care
Deodorant, Internal
Diaper Rash
Digestive Aid
Drink Overindulgence
Exocrine Pancreatic Insufficiency
Expectorant
Fever Blister
Food Overindulgence
Hair Growth and Loss
Hormone
Hypophosphatemia/Hyperphosphatemia
Ingrown Toenail
Insect Bite & Sting
Insect Repellent, Oral
Laxative
Leg Muscle Cramps
Male Genital Desensitizers
Menstrual
Nailbiting
Ophthalmic

Oral Health Care
Oral Wound Healing Otic
Overindulgence, Food & Drink
Pancreatic Insufficiency
Pediculicide
Poison Oak/Ivy
Poison Treatment
Prostatic Hypertrophy
Psoriasis
Seborrheic Dermatitis
Sedative, Daytime
Silver
Skin Bleaching
Skin Protectant
Sleep Aid, Nighttime
Smoking Deterrent
Stimulant
Stomach Acidifier
Sunscreen
Thumbsucking
Topical Analgesic
Vaginal Contraceptive
Vaginal Drug Products
Vitamins & Minerals
Wart Remover
Weight Control



More Ingredients

risedronate sodium
crospovidone
ferric oxide yellow
hydroxypropyl cellulose
hydroxypropyl methylcellulose
lactose monohydrate
magnesium stearate
microcrystalline cellulose
polyethylene glycol
silicon dioxide
titanium dioxide



stannous fluoride
glycerin
hydrated silica
sodium hexametaphosphate
propylene glycol
PEG-6
water
zinc lactate
trisodium phosphate
flavor
sodium lauryl sulfate
sodium gluconate
carrageenan
sodium saccharin
polyethylene
xanthan gum
titanium dioxide
blue 1



Used Longer



Used for diagnosed conditions



Used for life...
as long as you have teeth



Doses Larger



Once weekly
240 mg per dose
240 mg per week
11.5 g per year
12 refills

Twice daily
2 g per dose
140 g per week
1.4 kg per year
8 refills (6 oz tubes)



Cost Less



\$89 per refill
\$1064 per year
\$92 per gram



\$4 per tube
\$32 per year
2¢ per gram



Same Rules...Different Conditions

More ingredients in larger amounts

Broader distribution and use

Tighter profit margins

Pressure to keep costs down

More market competition

Huge emphasis on product quality and safety



Implement? ICH & USP Teach...

Testing of drug substances, excipients, and drug products for residual solvents should be performed when production or purification processes are known to result in the presence of such residual solvents. It is only necessary to test for residual solvents that are used or produced in the manufacture or purification processes.

**This makes sense! Only look for things that are likely to be there!
How do we know what is likely to be there? Certainly the supplier knows best. Is FDA OK with this?**



Implement? ICH Teaches...

Manufacturers of pharmaceutical products need certain information about the content of residual solvents in excipients or drug substances in order to meet the criteria of this guideline. The following statements are given as acceptable examples of the information that could be provided from a supplier of excipients or drug substances to a pharmaceutical manufacturer:

Only Class 3 solvents are likely to be present. Loss on drying is less than 0.5%.

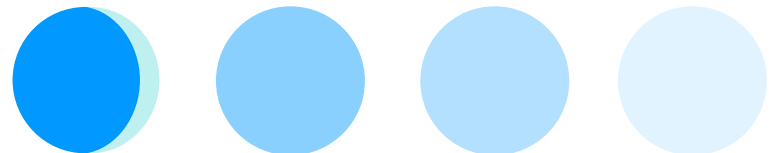
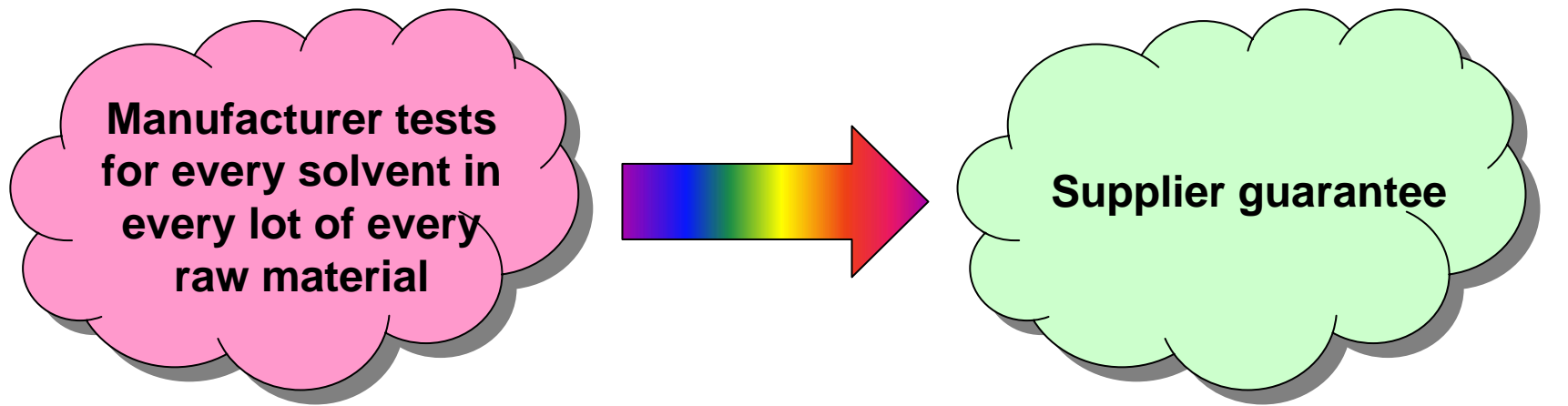
Only Class 2 solvents X, Y, ... are likely to be present. All are below the Option 1 limit. (Here the supplier would name the Class 2 solvents represented by X, Y, ...)

Only Class 2 solvents X, Y, ... and Class 3 solvents are likely to be present. Residual Class 2 solvents are below the Option 1 limit and Class 3 solvents are below 0.5%.

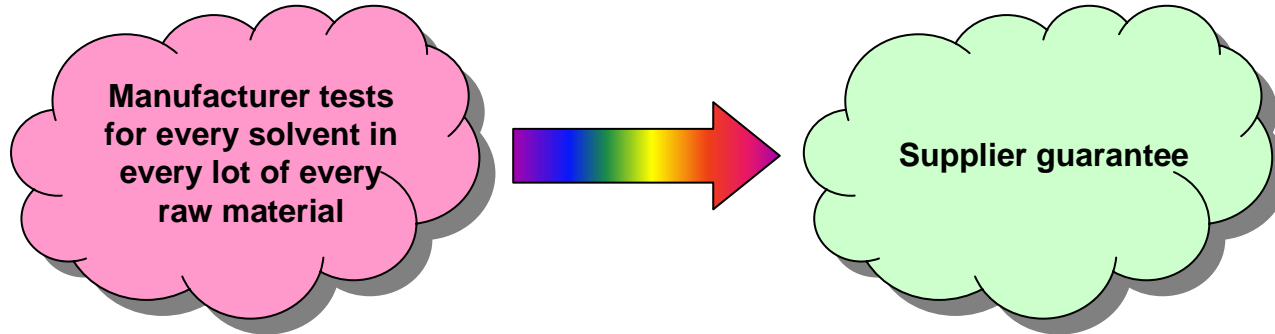
Are supplier guarantees an acceptable part of implementing the residual solvent guidelines?



Implementation Spectrum



Business Impact



Increased testing
Increased costs
Increased prices
Lower competitive edge
Reduced risk

Minimal testing
Minimal cost increase
No product cost impact
Same competitive edge
Increased risk



Discussion Points

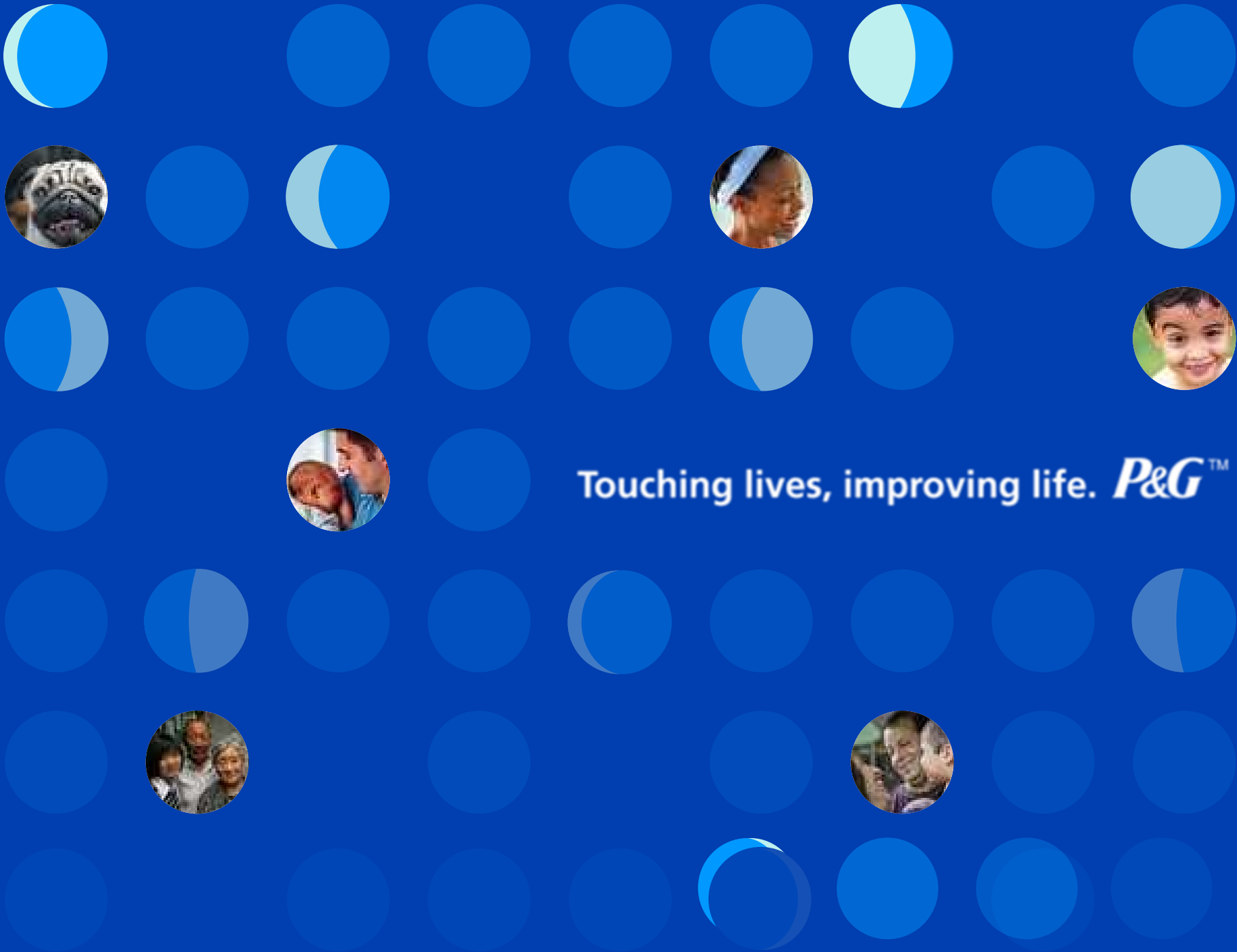
Who is responsible for compliance with USP residual solvent guidelines?

- Supplier
- Manufacturer
- Both?

How far can manufacturers take supplier guarantees?

Who is going to validate all these methods?





Touching lives, improving life. *P&G*™



U.S. PHARMACOPEIA
The Standard of QualitySM

Thank You

