Michael Simpson, Ph.D. has over 20 years of experience in Consumer Healthcare R&D. He has Ph.D. in chemistry from Heriot Watt University and began his career with P&G in the UK before moving with them to the US in 2006. Michael has focused on delivering consumer driven design, developing products in Oral Care for brands such as Crest, Cold products for Vicks, Pet Food for Iams as well as exploring new business development opportunities. In 2014 Michael joined Pfizer Consumer Healthcare with R&D responsibility for Centrum, Emergen-C and Caltrate.

He is now Chief Technology Officer for Santa Cruz Nutritionals, driving innovation in the rapidly growing nutritional gummies segment and exploring new opportunity areas.
Chewable Gels are a complex and challenging system

USP is developing a series of monographs to provide needed guidance for chewable gels:

- Ascorbic Acid Chewable Gels –Submitted to PF 43(3) [May-Jun, 2017]
- Cholecalciferol Chewable Gels –Submitted to PF 43(3) [May-Jun, 2017]
- Cyanocobalamin Chewable Gels –Submitted to PF 44(3) [May-Jun, 2018]
- Oil-and Water-Soluble Vitamins with Minerals Chewable Gels –Under development, target PF 44(6) [Nov.-Dec. 2018]

I’d like to discuss:
- The specificity of the analytical methods
- Follow-up on this mornings discussion ref lower label claims
**USP Monograph method**

**Ascorbic Acid Chewable Gels**

**DEFINITION**
Ascorbic Acid Chewable Gels contain ascorbic acid (C₆H₈O₆), sodium ascorbate (C₆H₇O₆Na), calcium ascorbate dihydrate (CaC₆H₇O₆.H₂O), or their mixture in an amount equivalent to NLT 90.0% and NMT 150.0% of the labeled amount of ascorbic acid (C₆H₈O₆).

**IDENTIFICATION**
- A. The retention time of the major peak of the Sample solution corresponds to that of the Standard solution, as obtained in Strength.

**STRENGTH**
- Procedure

  [Note—Use amber, low-aqueous glassware. Use cryogenic gloves when handling liquid nitrogen.]

  Extracting solution: Dissolve 73 g of metabisulfite acid in 800 mL of water, add 84 mL of glacial acetic acid, and dilute with water to 1000 mL.

  Mobile phase: 7.8 g/L of monobasic sodium phosphate dihydrate in water. Adjust with phosphoric acid to a pH of 2.5.

  [Note—Wash the column periodically with methanol and water using appropriate gradients to elute retained substances and avoid carryover interferences.]

  Standard stock solution: 1 mg/mL of USP Ascorbic Acid RS in Extracting solution. [Note—Sonicate with intermittent shaking to help dissolve, if necessary. Prepare fresh every time.]

  Standard solution: Dilute Standard stock solution with Extracting solution to obtain a solution containing 0.05 mg/mL of USP Ascorbic Acid RS.

  Sample solution: Immense 25–30 Chewable Gels in liquid nitrogen in a cryogenic vessel for 10 min. Cool a blender jar by swirling liquid nitrogen for about 1 min and discard the contents. Add frozen Chewable Gels to the cooled blender jar and grind to a fine powder. Transfer a portion of the powder, nominally equivalent to 25 mg of ascorbic acid, into a 25-mL volumetric flask. [Note—Proceed to this step immediately or keep the powdered Chewable Gels frozen until use.] Add 15 mL of Extracting solution, mix on a vortex mixer until well mixed, and sonicate for 10 min or until the sample has completely dissolved. Cool the solution to room temperature, dilute with Extracting solution to volume, and mix well. Quantitatively dilute a portion of the solution with Extracting solution to obtain a solution containing 0.05 mg/mL of ascorbic acid. Mix and pass through a 0.45-µm glass microfiber filter, discarding the first few milliliters of the filtrate.

**Chromatographic system**
(See Chromatography (621), System Suitability.)

  Mode: LC
  Detector: UV 245 nm
  Column: 4.6 mm x 15 cm; 3.5-µm packing L7
  Flow rate: 0.8 mL/min
  Injection volume: 10 µL

**System suitability**
- Sample: Standard solution
- Suitability requirements
- Relative standard deviation: NMT 2.0%

**Analysis**
- Samples: Standard solution and Sample solution
- Calculate the percentage of vitamin C, as ascorbic acid (C₆H₈O₆), in the portion of sample taken:

\[\text{Result} = \left(\frac{r_U}{r_S}\right) \times \left(\frac{C_S}{C_U}\right) \times 100\]

  \[r_U = \text{peak area of ascorbic acid from the Sample solution}\]
  \[r_S = \text{peak area of ascorbic acid from the Standard solution}\]
  \[C_S = \text{concentration of USP Ascorbic Acid RS in the Standard solution (mg/mL)}\]
  \[C_U = \text{nominal concentration of ascorbic acid in the Sample solution (mg/mL)}\]

**Acceptance criteria:** 90.0%–150.0%
Definition of a single USP method for a nutrient in all chewable gels will be a challenge.

Analytical method are developed to be reliable and repeatable.
• Typically they are developed and validated for a specific nutrient in a specific matrix, as per the approach used in drugs.

Chewable gel’s use a wide variety of matrixes e.g.
• Gelatin, Pectin, Starch, Locus Bean Gum etc.

Chewable gel’s also contain multiple complex ingredients e.g.
• Fiber, Fish Oil, Flavors etc.

Encapsulation is used to address stability challenges
• This can require us to develop or adapt a new analytical method to deliver the accuracy and repeatability necessary for compliance.

These complexities require the flexibility to develop new or adaption of existing analytical methods to ensure compliance
Minimizing Chewable Gel Overages

In the summary of last year’s USP Dietary Supplements Stakeholder Forum a comment was captured related to chewable gels.

‘Due to stability issue, manufacturers add an excessive amount of the nutrients during manufacture to compensate for loss during storage and achieve the declared shelf-life’

I would like to go back to the discussion earlier today reference overages and the proposal to:

Match the lower allowable label claim to drugs at 90%.

This would benefit all consumers of supplements with reduced overages. It would also enable reduction of overage in this consumer preferred and extremely complex delivery form of chewable gels.