The Gelatin Manufacturers Institute of America's (GMIA) Perspective on Melamine

The USP Excipients Stakeholder's Forum
Meeting #2
Wednesday, June 18, 2014
USP Headquarters, Rockville, MD

Gelatin is a Pure Protein

- Maximum 15% Moisture
- Maximum 2% Minerals

- Forms a thermo-reversible gel with unique gelling and visco-elastic properties.
- Primary use in Pharmaceutical industry is capsule manufacturing.
- Most important characteristics in gelatin specifications are Gel Strength (Bloom) and Viscosity.

Benefit of Adulterating Gelatin with Melamine?

- Gelatine has a high protein content; therefore, a high nitrogen content.
- Melamine is a nitrogen-based compound.
- Theory: Melamine could be used to bolster the apparent protein (nitrogen) content of gelatin.

Gelatin Industry has no Incentive to Adulterate Gelatin with Melamine

1. Gelatin is *not* sold to the pharmaceutical industry on the basis of protein content (weight).
2. The Gel Strength and Viscosity of gelatin are negatively impacted when adulterated by the addition of melamine.
3. Melamine is visible when mixed with gelatin in dry form, liquid solution and gelled solution.
4. Other “barriers to entry” are currently in place to prevent or detect such contamination.

Gelatin is not sold on Protein Content

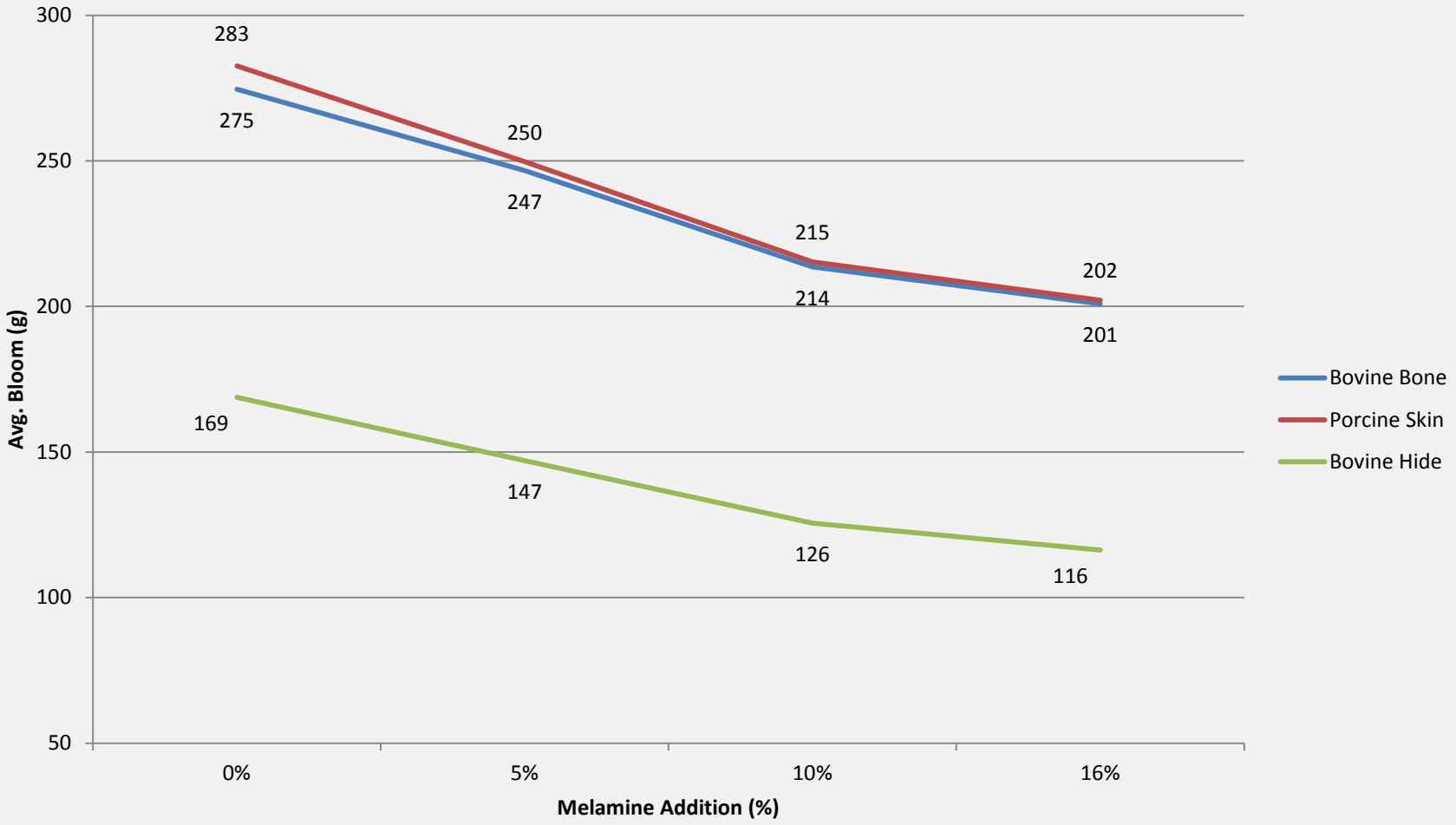
- Evidence:
  - A 2010 global survey of gelatin trade association members accounting for 85% of pharma grade gelatin sales, determined that *none* was sold on the sole basis of protein content.
  - Capsule manufacturers do not commonly require protein content to be reported on Certificates of Analysis (examples provided to the FDA in December 2012).

- Conclusion: Gelatin manufacturers sell gelatin to pharma/capsule companies on basis of weight of gelatin and other physical properties, not protein content.

Gel Strength and Viscosity are adversely affected by the addition of melamine

- Gelatin is valued for its protein structure which determines gel strength and viscosity.
- Replacing gelatin with melamine has an adverse affect on these properties and increases the variability of this testing.
- Technical Report: “The Impact of Melamine Spiking on the Gel Strength and Viscosity of Gelatin.” – Conducted to assess this impact.
- Results clearly indicate that these properties are significantly, negatively impacted on all gelatin types and raw material origin.
- This effect on gel strength is far greater than pure dilution alone.

Gel Strength and Viscosity are adversely affected by the addition of melamine



Melamine is visible when mixed with Gelatin

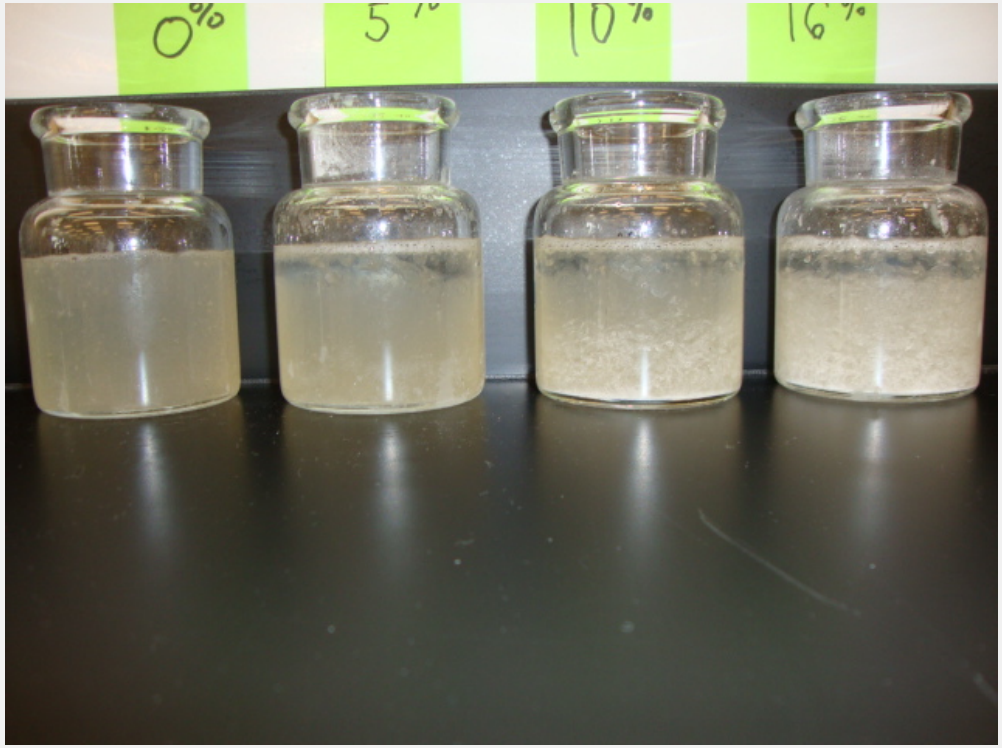
- During the technical study, samples were observed in the laboratories.
- The ability to see melamine when mixed with gelatin was apparent throughout the experiment.

Dry Gelatin with Melamine

- Melamine is bright white and fine grained.
- Gelatin is yellow and typically coarser for pharmaceutical/capsule applications.

Liquid Suspension of Gelatin with Melamine

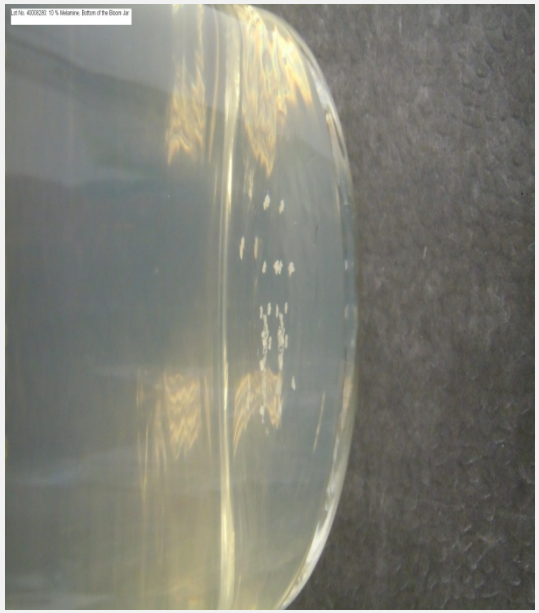
- The first step in preparing gelatin for capsule manufacturing is to mix the gelatin with water to form a liquid suspension (30-35% gel:water).
- This is also done as the first step in testing gel strength and viscosity (6.67% gel:water).



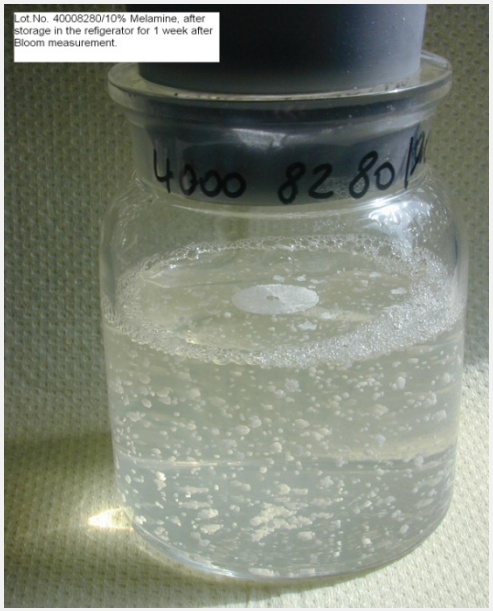
Gelled Form of Gelatin with Melamine

- Capsules are formed once the gelatin solution has solidified (gelled).
- This same concept is applied during gel strength testing.
- Melamine crystalizes in the gel and crystallization increases with time.

One Day w/10% Melamine



One Week w/10% Melamine



Other Barriers to Entry

- Capsule Manufacturers' Quality Requirements and strict GMP's would detect melamine contamination
  - Source gelatin from qualified manufacturers
  - Require Certificates of Analysis for each purchase/shipment of gelatin
  - Conduct in-house or qualified QC testing of gelatin raw material
    - QC Lab would easily note the presence of melamine during current USP/NF identification testing
  - Strict internal specifications
    - During capsule manufacturing, a large tank of 30-35% gelatin:water solution is prepared. Presence of melamine would be visually evident. Additionally, crystallization would be evident upon cooling.
  - Final QC examination and testing of final capsules
    - Capsules would have leakage problems due to holes or weak sections caused by melamine.
    - Visual inspection would detect melamine crystals.
    - Both scenarios would lead to rejection of capsules.

Conclusion

- There is no economic incentive for adulterating gelatin with melamine as gelatin is not sold on protein content.
- There is no product performance benefit gained by adulterating gelatin with melamine. Only performance detriment.
- The GMIA believes that the current harmonized USP/NF monograph and the testing therein provides an effective base for ensuring the safety and quality of gelatin. Therefore, the inclusion of a new identification test specific for melamine is not necessary to ensure the safety and quality of gelatin.