Delivering on Quality

A Manufacturer’s Perspective
February 23, 2021
Agenda

Hand Sanitizer Production
The Perrigo Story

- Timeline
- Development/Formulation
- Analytical Methods
- Packaging
- Stability Strategy
- Exhibit Batch
- Commercial Production
- Site Transfer
- Alcohol ID Guidance
- Donations
The Perrigo Story

From Conception to first Donations

30 Days

Initial request to develop formula
Lab Scale Formulation
Exhibit Batch
PNY Campaign #1 First 10 batches Manufactured / Packaged
Batches released and donations shipped

March 11, 2020
March 19, 2020
April 10, 2020
Timeline continued

Continued Production for Donation

- **PMI Transfer** (April 2020)
- **PNY Campaign #2** (May 2020)
- **PMI Campaign #1**
- **PNY Campaign #3** (June 2020)
  - (Final Release 06/18/20)

99 days after initial request!
**Development Path**

**FDA Guidance Formula vs New Product Development**

- **Option 1:** FDA Guidance “Policy for Temporary Compounding of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency”
  - EtOH/IPA, Glycerin, Hydrogen Peroxide, Purified Water
  - Pros: formula given in guidance, no pre-market stability, no expiration dating concerns.
  - Cons: Formulation is a liquid (product difficult to use & to control dosing), No existing internally approved H₂O₂ material.

- **Option 2:** Develop a gel-based formula
  - Pro: Product easy to use, familiar to users (most commercially available personal hand sanitizer products are gel-based), use of existing RMs.
  - Con: Requires formulation work, pre-market stability.

- Perrigo opted to develop a gel-based formula.
Perrigo New York Formulation R&D

- A partially developed formula from the 1990’s was used as a starting point.
- Suitable Raw Materials selected from materials already approved at PNY.
  - 1 RM was inactive, however previously used/approved
- RM orders were expedited
- 10 lab scale batches were made to further develop formulation.
- Batch size limited by safety concerns with flammability of EtOH.
- Process optimization – batch card updates were occurring until day of exhibit batch.
  - Alcohol concentration was key, calculation based on 190 proof RM
  - Screen added to ensure clarity of product
Analytical Development

Perrigo Michigan Analytical R&D

- Analytical method for EtOH was developed
  - Biggest obstacles
    - Time
    - First product samples received < week prior to exhibit batch
    - Robustness and consistency of methodology due to gel formula components

- Expedited documentation for method/specifications prior to testing exhibit batch
- Expedited EI assessment
- Analytical Method Validation Plan
- Exhibit Batch and Stability Testing Plan
Packaging Development

- Use existing components
  - 2 oz Bottles & Caps

- 6 bottle/cap configurations packaged for exhibit batch
  - 3 bottles, 2 caps (w/ and w/out induction seal)
  - All evaluated for stability

- 1 bottle chosen, both caps for commercialization

- Additional external 8-12 oz pump bottle options evaluated
Manufactured March 19, 2020

Exhibit Batch size: 300 kg

Cleaning Validation Waived
- Toxicity, Solubility, API volatility, Comparable RM use in other formulations, etc.

Packaged into 6 configurations

Method transfer not yet complete
- Batches tested at PMI AR&D lab

All configurations placed on Stability
Stability Strategy

Expedited Approach

- Stress stability (50°C/75% RH)
- Formal stability (40°C/75% RH & 25°C/60% RH)
- Stability Trend extrapolation based on available data from completed stations
- Shelf life extended as more data was available (3 month → 6 month → 16 month)
- Bulk Stability
  - Tested concurrently, 2 months
  - Forward thinking – donation batches prepared directly prior to filling
Campaign #1

- Scale-up to 1500 kg batch size (~25k bottles)
- Initial campaign of 10 batches – manufactured 03/26-04/07
- First 3 were Validation batches - Both cap options challenged during validation
- At-risk pending stability assessment / shelf life
  - 1st stability assessment / shelf life justification complete 04/09/20 – assigned 3-month expiry
- Method transfers to PNY from PMI
- Testing of commercial batches performed at both locations to expedite release
- April 10: 1st donations shipped & employee distribution (6 of 10 batches released)
- Full campaign released by 04/13/20
2 additional campaigns of 10 batches each

- **Campaign 2**
  - 6-Month Expiry
  - Manufactured 04/30-05/07
  - Released 05/11-05/15

- **Campaign 3**
  - 16-Month Expiry
  - Manufactured 06/04-06/12
  - Released 06/16-06/18
Formula Site Transfer

- ~8 Lab scale batches to optimize process for PMI equipment
- 1 Full Scale R&D Batch
  - Scale up to 4,210 kg (~70k bottles)
- RM Transfer
  - Shortage of denatured alcohol / No equivalent RM at PMI
    - Denatured existing EtOH RM w/ IPA
  - Use of equivalent RMs approved at PMI
  - Expedite approval and documentation for using PNY RMs at PMI
  - Materials transferred from PNY for batch execution
- Challenges based on moving to a liquid filling line
  - Diameter of Piping
  - Evaluation of Pump
- Stability Waiver Justification
1 Campaign for Donations

- Initial campaign of 2 batches (manufactured 05/06 & 05/12)
  - Limited based on donation need in areas
- 6-month Shelf Life
- Overcame ongoing challenges due to novelty of gel-based formula for the site
- Method transfers to PMI QC
- Testing of batches performed in both AR&D & QC to expedite release
- Released on 05/21 & 06/11
Special Considerations for Alcohol

Policy for Testing of Alcohol and Isopropyl Alcohol for Methanol

- FDA Guidance – January 2021
  - ID testing for Methanol, NMT 200ppm
  - ID on each container received
    - Drums vs. Tankers have significantly different lab burdens
  - FP method should distinguish between Ethanol (or IPA) and Methanol

- USP monograph for Alcohol updated to include this ID test

- USP monograph for Isopropyl alcohol not yet updated, however FDA guidance specifies to apply the 200 ppm limit for this as well.

- FDA guidance is for Ethanol/Isopropyl alcohol – not only in relation to hand sanitizer.
Hand Sanitizer Donations

By June approximately 1 Million Units were donated!

- 1st Responders
- Employees
- Hospitals
- Shelters
- Food Pantries
- Charitable Organizations
Celebrating Success

To commemorate this momentous achievement, Perrigo distributed framed awards:
- Over 225 Individual Contributors
- Across Many Departments
- From NY to MI to Ireland
Questions

Empowering a healthy tomorrow