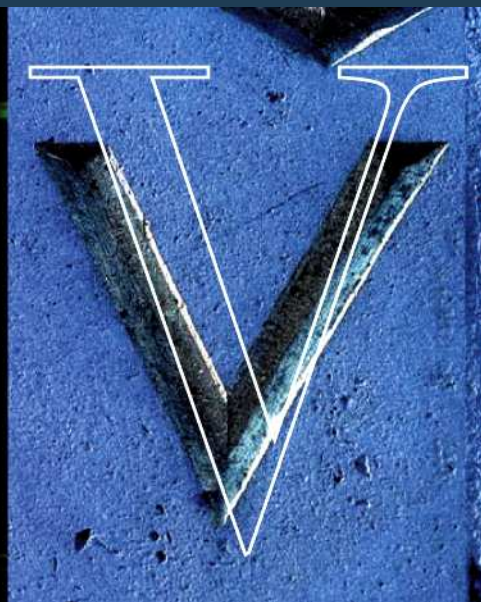
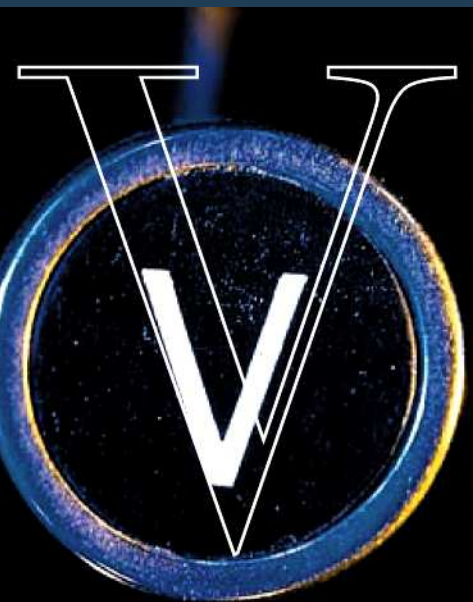


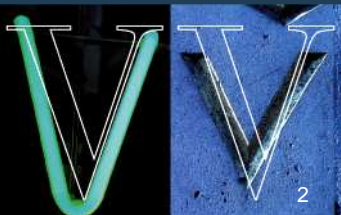
VENABLE[®]_{LLP}

Creating SOPs Under the Final GMP Rule to Assure the Identity, Purity, Strength, and Composition of Your Product



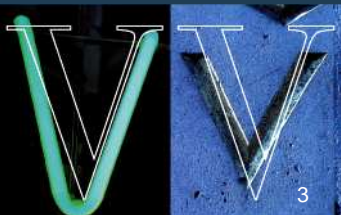
Presentation Overview

- Compliance: Who?
- Strategies for melding GMPs into SOPs
- Strategies for product testing
- Maintaining value while implementing
- Monitoring remote operations
- Effects of GMP-compliance on supply chain



Read the Federal Register – Then Write SOPs

- 72 FR 34751 – 34958
 - p. 34761 Overview (FDA intent)
 - p. 34764 Highlights (requirements)
 - p. 34789 Comments & Responses
 - p. 34915 Paperwork (expectations?)
 - p. 34932 Costs (expectations?)
 - p. 34942 List of (Final) Subjects
 - p. 34943 The (Actual) Rules



Compliance: Who?

- “If you manufacture, package, label, or hold a dietary supplement...”
 - Definition from Bioterrorism Act
- Applies to:
 - all domestic and foreign companies.
- Does not apply to:
 - companies that only manufacture or hold dietary ingredients.
 - companies only involved in harvesting, distribution or storage of agricultural commodities for incorporation into dietary supplements.
 - retailers that hold supplements for direct to consumers sales.

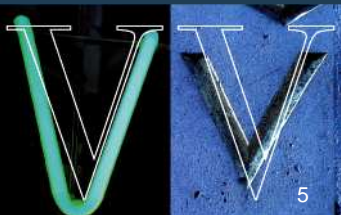
21 CFR Subpart A § 111.1

Melding GMP into SOPs – Step 1

■ Master the GMP Definitions

Watch for nuances, contrasts,
connotations

component → maintain *lot* control
(packaging items, too)
contact surface → know when to *sanitize*



Melding GMP into SOPs

- SOPs are required for
 - Subparts B thru D
 - Subparts F, G
 - Subparts J thru O
- SOPs not required
 - Subparts E, H, I, P



72 FR 34774

Melding GMP into SOPs

■ SOP Documents

- If electronic, must comply → 21 CFR 11
- Written records are acceptable!
- There must be Document Control
- There must be Change Control
- QC must authorize SOPs, approve tests

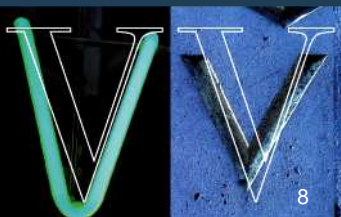
“must” v “shall” must = a requirement
“includes” = “includes, but is not limited to”



Testing & Quality Control

Example: Any qualified and/or experienced person not involved with or responsible for a given operation, can be trained and assigned to Quality. 21 CFR 111.12

Example: If a dietary ingredient is of land-based plant origin, “it is not likely you would include a limit on cadmium because cadmium is not a common contaminant of land-based plants.”



Testing & Quality Control

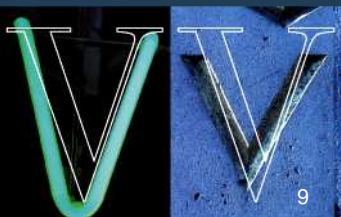
- Acceptable Test Methods
(used properly and consistently)

For ID:

Compendial Methods (USP, AOAC, FCC, JP, BP, EU, etc.), TLC, IR, HPLC, Mass Spec., ICP/MS, GC, HPLC, CE, Botanical ID, others

For Quantitative:

HPLC, GC, ICP/MS, CE, Compendia, others



Testing Product In-Process

- Control Points (21 CFR 111.70)
 - “in process”
 - “any point, step, or stage”
 - “where control is necessary to help ensure that specifications are met”

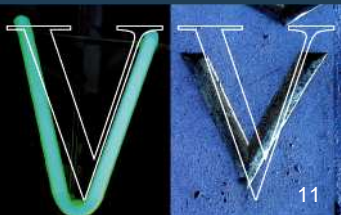
- HACCP v CGMP (21 CFR 111.75)
 - HACCP: focus, anticipate, act to prevent
 - GMP: directs required prevention steps



Testing Complex Formulas

- Use in-process assays to advantage
 - Graduated blending
(multiple blends, additive per batch)

Micro-ingredient blends can be assayed prior to incorporation with other ingredients in a Batch. Then weight reconciliation can bring the assay into context for confirming identity, purity, strength and composition of the finished dosage.



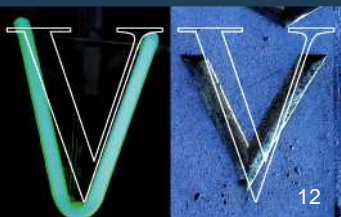
Optimizing \$\$ While Implementing

- Use what you already have: History
 - Reliable Master Formulas
 - Archived Batch Records
 - Retained Samples
 - Lab Records & Product Assays

Retrieve, Review, Analyze!

For writing unique Master Manufacturing records.

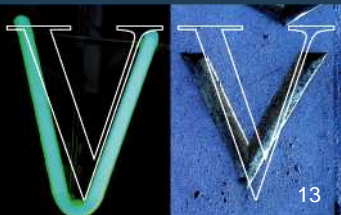
72 FR 34954 | 21 CFR Subparts H & I



Optimizing Compliance Costs

- Inspect your processors
 - Ask for GMP compliance presentations
 - Have multiple contacts (know QC)
 - Look for independent 3rd party audits
 - Consider a consultant
 - Join a trade association

Ask everyone what they have to help you!



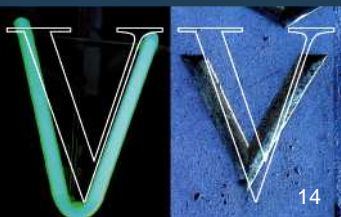
Qualifying Components & Suppliers

- Questionnaires & Surveys
(Instead of developing your own)
 - SIDI: Standardized Information on Dietary Ingredients



(joint effort: NPA, CRN, CHPA, AHPA)

- IPEC: International Pharmaceutical Excipients Council



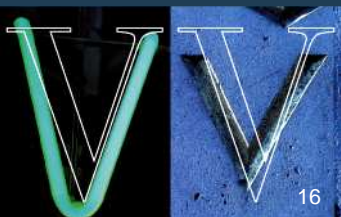
Monitoring Offsite Operations

- Be prepared for “routine” repetition of inspections, approvals, etc.
every 1 – 2 years or more frequently.
- Set up systems that are efficient and questionnaires that can be returned easily. Weigh the burdens carefully.



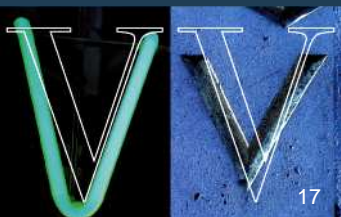
Effect of GMP-compliance on Supply Chain

- Tap suppliers for full value
 - Information
 - Lab support
 - Assay methods
 - Training and orientation
 - Support for QC issues



Effect of GMP-compliance on Supply Chain

- Today's business environment
 - Tight supply on basics
 - Olympics & China
 - Lack of profitability
 - Increased costs
 - Raw materials
 - Energy & transportation
 - Ingredients of petrochemical origin
 - Food Supply v. Energy Supply



Effect of GMP-compliance on Supply Chain

- Ultimately the entire supply chain will host higher quality standards in the face of competition.
- Consumers will gain confidence in Dietary Supplements made in the US.



Lessons Learned

- Incorporate all the rules!
 - Do you need international compliances?
 - Include all US regulations – still required

FFD&C (NLEA, DSHEA)

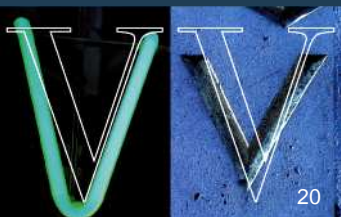
FQPA (FIFRA)

Bioterrorism, FALCPA, NOP, AER, etc.



GMP: Creating Sound SOPs

- ✓ Use what you already know (history)
- ✓ Everyone needs to know the GMPs
- ✓ Go for audits; use smart questionnaires
- ✓ Strive to be “consistent”
- ✓ Remember all the rules (not just GMP)
- ✓ Read the CFR & the Federal Register



Assuring Key Aspects of Your Product

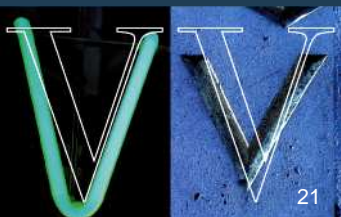
Identity

Purity

Strength

Composition

**Quality is
Engineered from
the Start**



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