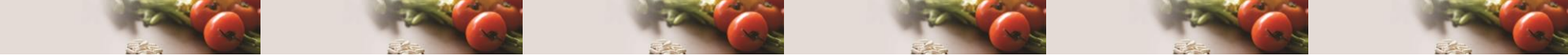

Dietary Supplements: Finished Product Specifications, Serious Adverse Events (SAEs), and More

Jonathan M. Cohen, Partner, K&L Gates LLP

Tara Lin Couch, Ph.D., Senior Director, Dietary Supplement and Tobacco Services, EAS Consulting Group

Moderated by Robert Durkin, Of Counsel, Arnall Golden Gregory LLP

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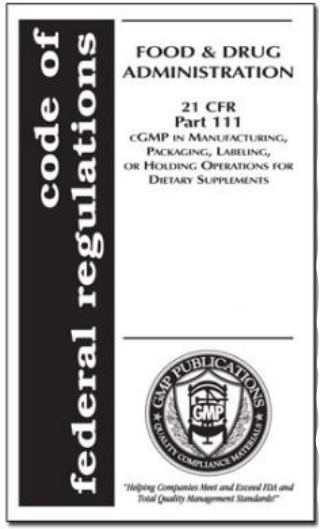
Agenda(!)

“Dietary supplements continue to thrive as consumers become increasingly health-conscience and health-focused. Panelists will address an array of considerations for dietary supplement manufacturers, including:

- *Nutrient content claims;*
- *Verifications;*
- *Complaint monitoring;*
- *Reporting SAEs;*
- *Conducting recalls;*
- *Third-party contracting; and*
- *Insurance.*

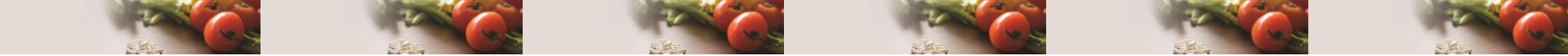
Quality Systems



- 21 CFR 111, *Current Good Manufacturing Practice in Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements.*

- GMP regulations requires a **Quality System** of procedures and documentation for the proper design, monitoring, and control of manufacturing processes and facilities to ensure finished products have the identity, strength, quality, and purity that they are represented to possess.
  - A cGMP Quality System enables companies to minimize or eliminate instances of contamination, mix-ups, and errors.

  ⇒ *These are the reasons for dietary supplement product complaints.*



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Finished Product Specifications

- The establishment of Finished Product Specifications is, and has been the most cited FDA observation since 2010
- 2021 FDA Observations statistics indicate:
  - 40.1% cited 21 CFR 111.70(e): Specifications - identity, purity, strength, composition
  - 4.8% cited 21 CFR 111.70(e) Specifications - contamination limits
- 21 CFR 111.70(e): For each dietary supplement that you manufacture you must establish **product specifications** for the identity, purity, strength, and composition of the finished batch of the dietary supplement, and for limits on those types of contamination that may adulterate, or that may lead to adulteration of, the finished batch of the dietary supplement to ensure the quality of the dietary supplement

TOP FDA Observations: 2010 - 2021

Item	Description	Observations Cited												
		2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2010-2020	%All
1	Specifications	32	104	176	234	204	154	214	247	226	236	150	155	**2132**	**13%**
2	Testing	54	111	226	287	188	144	195	213	171	157	95	91	**1932**	**11%**
3	MMRs	28	53	94	117	82	67	87	94	81	72	91	47	**913**	**5%**
4	BPRs	18	52	74	93	71	71	72	84	84	69	115	59	**862**	**5%**
5	QU Operations	18	43	47	66	47	45	55	73	59	74	125	134	**786**	**5%**
	Total Observations	631	1328	1964	2211	1549	1294	1625	1795	1553	1433	868	739	**16990**	**39%**

Serious Adverse Events

- **Adverse Event (AE)** - Any health-related event associated with the use of a dietary supplement that is adverse
- **Serious Adverse Event (SAE)** - An adverse event that results in:
  - Death;
  - A life-threatening experience;
  - Inpatient hospitalization;
  - A persistent or significant disability or incapacity;
  - A congenital anomaly or birth defect; or
  - that requires, based on reasonable medical judgment, a medical or surgical intervention to prevent an outcome described above.

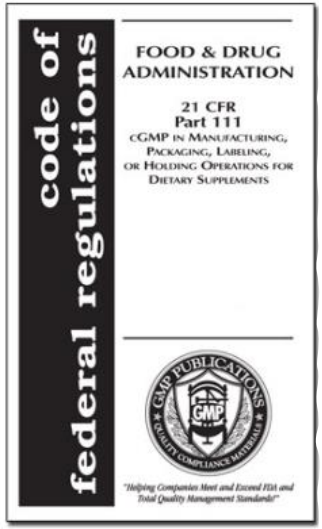
Product Complaints

- 2006 Dietary Supplement and Non-prescription Drug Consumer Protection Act
  - Requires the reporting of all SAEs to the FDA through the MedWatch system
  - Reports must be submitted within 15 business days of receipt
- Serious Adverse Events are received through a product complaint so all product complaints must be triaged to determine if there is any allegation expressing concern
  - 21 CFR 111.3: **Product Complaint** - Any communication that contains any allegation, written, electronic, or oral, expressing concern, for any reason, with the quality of a dietary supplement, that could be related to current good manufacturing practice

Product Complaints

- 21 CFR 111.560: A qualified person must investigate any product complaint that:
  - Involves a possible failure to meet any specification;
  - Requirement of 21 CFR 111; or
  - May present a risk of illness or injury
  - Investigation must extend to all relevant batches and records

Quality Systems



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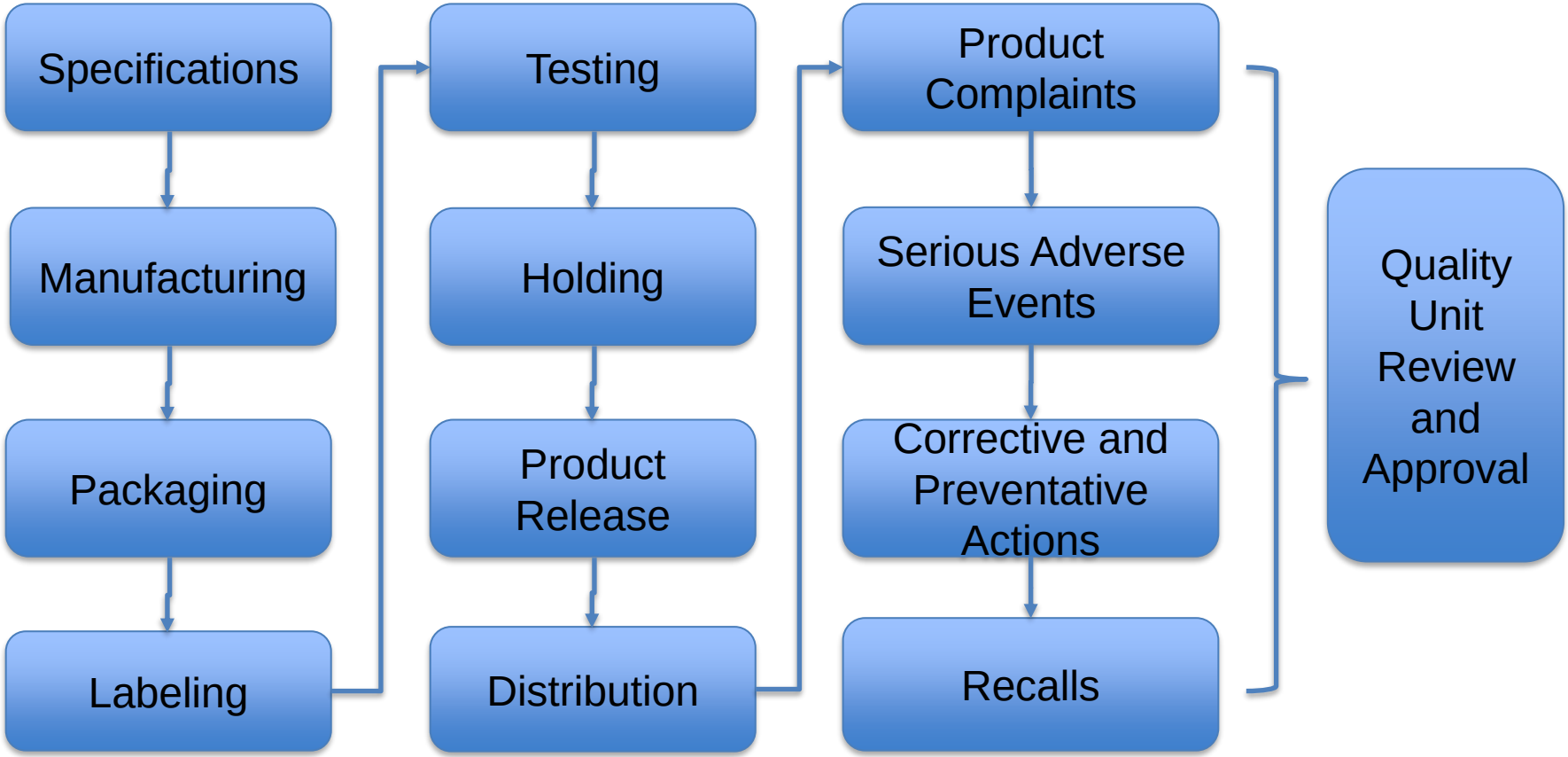
  ⇒ *These are the reasons for dietary supplement product complaints.*

Many…Quality Systems

- Numerous Quality Systems are involved from the establishment of finished product specifications through to the complaint system that will identify an SAE……More!

Finished Product Specifications ⇒ Serious Adverse Events


Specifications
Manufacturing
Packaging
Labeling
Testing
Holding
Product Release
Distribution
Product Complaints
Serious Adverse Events
Corrective and Preventative Actions
Recalls
Quality Unit Review and Approval

OLDs

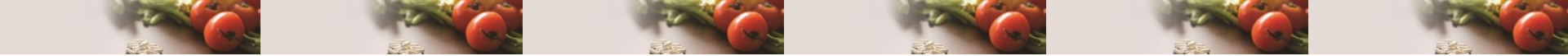
- All of these Quality Systems, particularly the establishment of Finished Product Specifications and the conduct of a Product Complaint Investigation; and potential reporting of Serious Adverse Events are further complicated by the contracting nature of the dietary supplement industry.
  - Contract Manufacturer
  - Contract Packager (Co-Packer)
  - Contract Laboratory
  - Distribution Warehouse
- **Own Label Distributor (OLD)** – Product brand owner that contracts with other firms to manufacture, package, and/or label product on their behalf for distribution to the consumer.

OLD GMPs

- Regardless of where operations take place, the FDA has made it clear that the OLD is responsible for compliance to all regulations to ensure:
  - Product is not adulterated
    - 21 CFR 111, *Current Good Manufacturing Practice (cGMP) in Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements*.
  - Product is not misbranded
    - 21 CFR 101, *Food Labeling*.
- .

OLD Warning Letters

- To the extent that you contract with other firms to manufacture, package, and/or label product on your behalf that your firm releases for distribution under your firm's name, **your firm has an obligation to know what and how manufacturing, packaging, and/or labeling activities are performed so that you can make decisions related to whether your dietary supplement products conform to established specifications and whether to approve and release the products for distribution**. [72 Fed. Reg. 34752, 34790 (Jun. 25, 2007)].
- Although a firm may contract out certain dietary supplement manufacturing, packaging, and/or labeling operations, it **cannot contract out its ultimate responsibility to ensure that the dietary supplement it places into commerce (or causes to be placed into commerce) is not adulterated** for failure to comply with dietary supplement CGMP requirements
  - United States v. Dotterweich, 320 U.S. 277, 284 (1943)
  - United States v. Park, 421 U.S. 658, 672 (1975)
- The FD&C Act **prohibits a person from introducing or delivering for introduction**, or causing the delivery or introduction, into interstate commerce a dietary supplement that is adulterated under Section 402(g) for failure to comply with dietary supplement CGMP requirements (see 21 U.S.C. §§ 342(g) and 331(a)).



WHAT SUPPLEMENT COMPANIES NEED TO KNOW ABOUT MANAGING RISKS THROUGH CONTRACTING AND INSURANCE

DIETARY SUPPLEMENTS: FINISHED PRODUCT SPECIFICATIONS, SERIOUS ADVERSE EVENTS (SAE's), AND MORE

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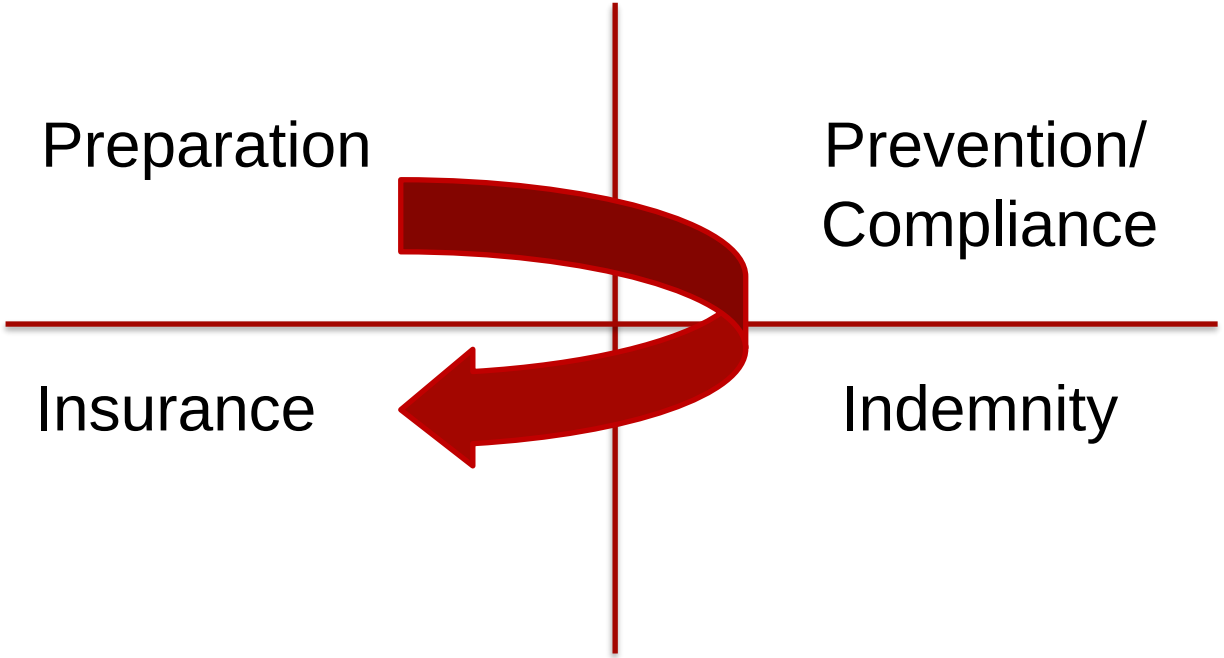
March 30, 2022

K&L GATES

FDLI

HOW TO THINK ABOUT RISK



SUPPLY CHAIN RISK IN THE SUPPLEMENT INDUSTRY

- Complexity of supply chains
- Impact of globalization and political risks
- Challenges of navigating supply chain disputes

KEY RISK MANAGEMENT PROVISIONS OF SUPPLY AGREEMENTS

- Benefits of formal agreements
- Representations and warranties
- Minimum insurance requirements
  - Types and amounts of coverage
  - Mandatory policy provisions
  - Proof of insurance/certificates of insurance
- Additional insured provisions
- Indemnity and recall management provisions

SOME SPECIAL ISSUES IN SUPPLY CHAIN DISPUTES

- Litigating with business partners
- Privilege and confidentiality issues
- Contractual privity and claims down the supply chain

KEY INSURANCE POLICIES

- Standard business policies
  - Property/business interruption
  - General liability
  - Directors/officers and errors/omissions
- Specialty policies to consider
  - Recall/contamination policies
  - Cyber-risk policies
  - Media liability policies
  - Transportation risk (cargo, marine, through-put)
  - Political risk

HYPOTHETICAL FOR DISCUSSION - CONTAMINATION OF SUPPLEMENT INGREDIENT RESULTS IN RECALL AND INJURIES

- Are indemnities implicated and implemented
- Whose policies might apply - additional insured provisions
- Do standard business policies apply
- What issues might arise in recall/contamination insurance claim
  - What is “contamination” and “impairment”
  - What is the bodily injury requirement
  - Known loss/intentional acts/defect exclusions
  - Causation issues in proving loss (“solely and directly”)
  - The battle of the accountants

HYPOTHETICAL FOR DISCUSSION - CONSUMER CLASS ACTION REGARDING REPRESENTATIONS REGARDING SUPPLEMENT HEALTH BENEFITS

- Are indemnities implicated and implemented
- Whose policies might apply - additional insured provisions
- Do standard business policies apply
- Specialty policy - media liability

THANK YOU !!!

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