

FDA Supplement Reductions under 21st Century GMP Initiatives

Calvin Koerner

I.Q. Auditing



Historical Perspective

- Vast Majority of Laws and Regulations were enacted because people were getting hurt (Broad Stroke)
- FDA's oversight/authority have been instrumental in achieving the current level of compliance
- Proactive FDA oversight is critical for Public Safety
- FDA's Mission and Legal Responsibilities serve to ensure Safe Public Health

Current Situation

- Manufacturer's may be hesitant to make process improvements due to the burdens of current Regs. and Policies. (broad micro-oversight, inflexible, and lowest common factor approach)
- FDA's Resources are limited and are stretched more each day
- Risk is not the likelihood of error, but potential/time
- Supplement review/approval is necessary, but is not always interpreted/implemented consistently

Implementing 21st Century GMPs

1. Reducing supplements across all companies by changing regulations and/or guidance documents
2. Encouraging volunteer implementation of “Design Space” for reduced supplements (new products)
3. Opening FDA Policies for acceptance of Master Development and Qualification Protocols for reduced supplements

calvin@iqauditing.com



Reg. Change Considerations

- Changing Regs. to reduce supplements across all companies assumes all companies and processes are equal, which they are not (broad macro-oversight)
- Current Regs. provide significant flexibility in their definitions. (Examples are restrictive)
- Targeted Reductions (more bang for the buck)
- Loosening Reg. definitions is likely to provide greater confusion/ambiguity

Reg. Change Cont.

- Reg. revisions may be controversial and time consuming
- The goal should be to reduce “*substantial potential to adversely effect product*”, not just supplement numbers
- Will not provide parallel systems to reward “Good Companies”
- Will transfer some oversight from being proactive to being reactive (nobody wins)

Design Space Considerations

- Allows each company and process to be evaluated individually (selective macro-oversight)
- Will provide parallel systems (B-micro/S-macro)
- Will provide greater manufacturing flexibility
- Removes ambiguity and substantially reduces “potential risks” with proactive approach
- Is mainly applicable to new applications

Design Space Cont.

- Regs. may need to be revised to provide application/definition clarifications
- Is likely to require significant upfront company resources
- Is likely to increase time to reach market
- Will be difficult to use as an enforcement tool

Master Protocol Considerations

- Master Development and Qualification Protocol
- Will provide greater targeted manufacturing flexibility with restrictions on scope and use (not blank check)
- Removes ambiguity and substantially reduces “potential risks” with proactive approach
- May be useful as an enforcement tool

Master Protocol Cont.

- Allows each company and process to be evaluated and rewarded individually (selective/dynamic macro-oversight)
- Is applicable to all products (new and licensed)
- Isn't likely to increase time to reach market
- Will provide parallel systems (B-micro/SD-macro)
- Can be implemented today with policy acceptance. Regs. do not need to be modified (314.70(e))

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Recommendations

- Current Regs. aren't bad, but should be tweaked
- Creating a better definition of “change” to eliminate items that don't need to be reported
- Limiting major, moderate, and minor change examples to Guidance Document
- Pursuing all three paths in parallel
- Training FDA foot soldiers on each path

Summary

- FDA Oversight is necessary and good
- FDA's Oversight grip could be loosened
- Broad targeted macro-oversight is okay
- Selective macro-oversight is better
- Selective/dynamic macro-oversight is best for all