QUARTERLY WHITE PAPER – ISSUE 01

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TEMPERATURE CONTROL

New GUI-0069 rules are coming for the Transportation & Storage Industries

Health Canada issues revision to GUI-0069

Health Canada issued a draft revised guidance for industry for consultation on December 20, 2018. As with all such draft revisions, the guidance was not generally distributed and was sent only by request to interested stakeholders for comment. As of this moment there has been no formal date set for release of a final guidance, however it is scheduled for 2020 release.

Does this impact you? The scope of the new guidance has not changed much; however the emphasis on risk and controls has been enhanced and covers the entire supply chain. If your business is part of the Pharma supply chain, chances are the revised guidance will affect you at some point. Interested parties include: 3PL, Transportation providers (ground, air, rail), depots, and "last mile" couriers.

More than Temperature Mapping – Supply chain control goes beyond traditional mapping (see Page 3).

The Rules Are Changing: The impact of revised Health Canada GUI-0069 "*The New Normal*"

Third Party Logistics ("3PL") provide various outsourced supply chain services including warehousing and distribution (e.g., delivery to customers) for their Pharma clients. They are viewed as an extension to the pharma business and have undergone regular regulatory scrutiny for more than 20 years, bearing the regulatory burden for those activities they provide.

Health Canada recognizes that potential supply chain hazards posed to pharmaceutical products are not limited to storage, but extend to transportation from manufacturers to 3PL partners, and from 3PL partners through an increasingly complex supply chain into the hands of patients. This has led to a revised approach to post-manufacturing environmental controls and scrutiny for pharmaceuticals, biologics, medical devices, animal health and natural health products. The result is an updated guidance with clearer expectations for all stakeholders. This White Paper will highlight and discuss some of the changes that can be expected, and will propose some solutions that may ensure the supply chain industry will be ready when the revised Guidance becomes effective.

Have you considered that in the journey of a finished drug product from a manufacturing site into the hands of patients, the drug product spends roughly two thirds of its time in-transit? Given the often limited shelf-life of such products, it makes no sense to have them sit in a warehouse for an extended period. Thus safety stocks are kept low and turnover high ensuring that most products reach the hands of consumers within a few short months from the time of manufacture. If one were then to profile the environmental hazards the products are exposed to, we can identify an entirely new set of risks for the supply chain, and for manufacturers and importers to be concerned about. So the question becomes: How well do you know your supply chain? Can you accurately describe the path your product takes? Do you know how many times the product is handled outside of your possession and before the customer receives it? Are you confident that there are appropriate controls and monitoring throughout? Let's look at a few of the changes and how they may affect you.

Principles for Inspection Success

There are a few principles to follow to ensure you have success in an audit or Health Canada Inspection.

Know your Supply Chain – Be able to describe it in detail, and demonstrate you know your sources of risk.

Understand Risk – Identification is not enough. You need to demonstrate you have controls in place and that they are effective.

Keep in mind that detection is not considered a control! Anything that reduces severity or likelihood of occurrence is wherein your value lies.

Qualify Equipment, Processes, and Controls – Ensure all are fit for their intended use, and keep clear and thorough documentation.

Well written documentation should tell the full story and need little or no explanation during an audit.

Know your work – Be able to explain it simply and completely. An audit will go much better if the auditor leaves with the impression that you have expertise in your field and know what you are doing. They need to leave with a sense that even if every little thing is not perfect, that you are *in control* and working to make things better.

Documented Agreements – Have these in place with involved supply chain parties covering responsibilities and mandated Quality requirements (QAA).

What you need to know about the changes

Understand them and then apply them

More prescriptive and plainer language – the new draft Guidance takes some pains to lend context to and clarify the intent of Health Canada's expectations. For simplicity, we will refer to the "old" Guidance (GUI-0069 April 28, 2011)[1] and "new" Guidance (GUI-0069 Draft December 20, 2018)[2].

For example, 3.2 (8) in the old Guidance requires that "*storage and/or transportation activities performed by sub-contractors be verified by reviewing documentation*". While this still infers that responsibility rests with the contract holder (distributor or seller), it is open to interpretation. By contrast, the new Guidance under 4.2 (2) states "*Make sure drugs are transported in accordance with established procedures. When using contracted third parties, it is your responsibility to ensure that they transport the drugs within the established procedures*". This is a very pointed difference in language, leaving little room for interpretation. Responsibility rests with the contract holder, not with the transport company. The expectation is that the contract holder ensures their transport provider follows procedure and also therefore, the Guidance. The new reality is that any failures on the part of a transportation partner rest fully with the contract holder (e.g. importer / seller).

"Clearer expectations, reduced ambiguity, assignment of responsibility!"

A controversial subject discussed within the new Guidance is the use of Mean Kinetic Temperature ("MKT"). Conspicuously absent in the old Guidance, it is nevertheless commonly used by the pharmaceutical industry to justify sale of drugs which were exposed to temperature excursions. While the Guidance does not discourage use of MKT it clearly suggests rules for its appropriate use and references USP <1079>[3] for additional guidance. Use of MKT can easliy become a slippery slope and it application can be easily misinterpreted when making quality decisions on products exposed to temperature excursions. Interpretation and application should be enshrined into an SOP, and quality decisions taken with great care.

These are just two examples of key differences in the approach Health Canada has taken to remove the guess-work and interpretation necessary to understand and apply a very important guidance, which is intended to protect consumers and assure a safe and effective drug supply.

So how does this impact the manufacturer or service partner? It makes expectations clearer, assigns responsibility, and casts light on formerly grey areas which were often dismissed or misinterpreted. More importantly, it provides you with a working list of requirements and expectations against which to measure your compliance.

Some important questions to ask within your organization: How well do we understand the guidance? Do we have any gaps, and if so what are they? Do we have the in-house expertise and resources to close knowledge gaps? How much is enough?

Compliance Solutions for Industry

Implementation of the new GUI-0069 expectations takes a little more than general knowledge.

It is now about more than temperature mapping, and the level of expertise required to truly understand and gain control needs to improve. Some recommended approaches to address this gap in expertise include:

Short-Term

1. Retain a known expert to help with identifcation of supply chain risks and gaps (knowledge, process, controls), remediation planning, and implementation for those items most critical to the safety of your or your customers' products.

Long-Term

2. Identify personnel within your organization that will be tasked with continuing and maintaining this effort.

3. Develop a Training program for Operations, Supply Chain, and QA with the key goal being knowledge transfer from the expert to your personnel.

4. Put in place policies and procedures to govern and guide your organization and and any vendors which may impact your overall process.

4. Periodically review progress using internal mini-audits as part of your self-inspection program.

5. Establish and monitor metrics of the process as part of Executive Management Review to ensure that quality and temperature control remain on the radar screen. After all, compliance should be a by-product of quality, not the goal and this needs to be embraced at the Executive level.

For more information, see Professional Resources.

Q: So when can I use MKT?

A: USP <1079>[3] states that MKT analysis may be used for storage conditions that have exceeded the acceptable parameters for a drug product, for a short period of time It is not intended to be a measure for long-term storage. Also, it is essential to know the upper and lower temperature limits of any excursion. Extreme temperatures outside of available stability data make it impossible to predict the quality impact of the excursion with any confidence. As a general rule, it is advisable to use MKT as only one method of assessing thermal stress on a drug product; for excursions over short durations and only when there is stability data available in support of the upper and lower range of the excursion (s). MKT is a single temperature and ought not to be used as the sole determining factor (e.g., it may not be appropriate in cases where liquids or suspensions are subject to phase change or separation, products that are biologics, or stability studies that indicate temperature excursions do indeed have an impact on product quality). In other words, use it carefully and err on the side of caution. MKT analysis must be based on good science and take into account the integrity of the product. Be sure you have a written SOP in place with clear guidelines for application of MKT in quality decision-making.

EYE ON IT

Have you considered…

1. An independent unbiased audit (gap assessment)?

At times having an outside perspective from an expert can offer new insight and taps into an experienced resource which may have meaningful and practical solutions to offer that have been proven elsewhere. A gap assessment can be a useful "health check" for you or your transportation vendor, and help to understand where environmental risks may exist that aren't always visible during a routine GMP surveillance audit.

2.Taking advantage of routine GMP audit feedback to implement a process of continuous improvement?

Routine surveillance audits can be a great source of "free consulting" if you know how to extract learnings and information from them. The most useful pieces are not the audit reports, but rather the line of questioning and intent of the questions asked. This can also be true when supplier management, environmental controls, and monitoring come under scrutiny. All are keys to ensuring a safe drug supply.

Professional Resources

Interested in knowing more about the forthcoming changes and how they affect you? Contact Skillpad Compliance and our experts will help ease the pain of change for your organization.

References

[1] **GUI-0069 Guidelines for Temperature Control of Drug Products during Storage and Transportation**

Health Products and Food Branch Inspectorate; Implemented April 28, 2011

[2] **GUI-0069 Guidelines for environmental control of drugs during storage and transportation**

Health Products and Food Branch Inspectorate; Draft issued December 20, 2018

[3] **USP Standard ⟨1079⟩ GOOD STORAGE AND DISTRIBUTION PRACTICES FOR DRUG PRODUCTS**

Note: USP is currently revising this standard, expect a new revision in 2020.

In Our Next Issue: Supply Chain Hazard Mapping – Understanding Risks

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