The Practice of Inference in the U.S. Pharmaceutical Supply Chain
# Table of Contents

ASSUMPTIONS ........................................................................................................................................... 2  
INTRODUCTION ....................................................................................................................................... 4  
THE PRINCIPLE OF INFEERENCE ........................................................................................................... 4  
INFEERENCE AS AN APPLIED CONCEPT ............................................................................................... 6  
APPLYING SERIALIZED INFEERENCE TO PHARMACEUTICALS IN THE SUPPLY CHAIN ...................... 6  
INFEERENCE IN ACTION IN THE PHARMACEUTICAL SUPPLY CHAIN .................................................. 8  
THE DECISION TO USE INFEERENCE .................................................................................................... 10  
APPENDIX: REFERENCES & RECOMMENDED READING ...................................................................... 13
Assumptions

This paper provides a general discussion on the topic of inference as it applies to the United States pharmaceutical industry. Suggestions presented in these materials are designed to provide a starting point for industry collaboration toward common solutions. They are not to be considered legal advice and are not intended to be a substitute for competent legal counsel. It is up to individual companies to comply with current U.S. state and federal regulations, and supply chain participants should rely on their own company’s legal counsel for legal interpretations of statutory and regulatory requirements.

These materials have been prepared based on the following assumptions:

- Readers are familiar with U.S. pharmaceutical supply chain practices
- Readers are familiar with overt security measures used in the U.S. pharmaceutical supply chain (e.g., manufacturer security tape, seals, holograms, etc.)
- Readers are familiar with current federal and state legislative and regulatory initiatives
- Readers are familiar with the Industry Adoption Task Force (IATF)

GS1 Healthcare US would like to thank the members of the Traceability Adoption Workgroup for their hard work and dedication in developing these materials.
About GS1®

About GS1®
GS1 is a neutral, not-for-profit organization dedicated to the design and implementation of global standards and solutions to improve the efficiency and visibility in supply chains. GS1 is driven by more than a million companies, who execute more than six billion transactions a day with the GS1 System of Standards. GS1 is truly global, with local Member Organizations in 108 countries, with the Global Office in Brussels, Belgium.

About GS1 US™
GS1 US is the Member Organization of GS1 that serves companies in the United States. As such, it is the national implementation organization of the GS1 System dedicated to the adoption and implementation of standards-based, global supply chain solutions in the United States. GS1 US currently serves over 200,000 U.S. member companies — 16,000 of which are in healthcare.

About GS1 Healthcare
GS1 Healthcare is a global, voluntary healthcare user group developing global standards for the healthcare supply chain and advancing global harmonization. GS1 Healthcare consists of participants from all stakeholders of the healthcare supply chain: manufacturers, wholesalers & distributors, as well as hospitals and pharmacy retailers. GS1 Healthcare also maintains close contacts with regulatory agencies and trade organizations worldwide. GS1 Healthcare drives the development of GS1 Standards and solutions to meet the needs of the global healthcare industry, and promotes the effective utilization and implementation of global standards in the healthcare industry through local support initiatives like GS1 Healthcare US in the United States.

About GS1 Healthcare US®
GS1 Healthcare US is an industry group that focuses on driving the adoption and implementation of GS1 Standards in the healthcare industry in the United States to improve patient safety and supply chain efficiency. GS1 Healthcare US brings together members from all segments of the healthcare industry to address the supply chain issues that most impact healthcare in the United States. Facilitated by GS1 US, GS1 Healthcare US is one of twenty four local GS1 Healthcare user groups around the world that supports the adoption and implementation of global standards developed by GS1.
Introduction

*Inference* is a topic of interest for stakeholders within the pharmaceutical supply chain.

What is inference?

Inference means “to derive as a conclusion based on facts presented.” It enables the supply chain partners to leverage strong business practices and relationships to meet daunting challenges which involve the verification of serialized (uniquely identified) items in shipping and receiving processes.

How is it applied in business?

Inference is common in the pharmaceutical industry today in a non-serialized context, often for safety and security reasons. It is also applied extensively within the consumer packaged goods industry.

Inference is applied as a business practice when a collection of items is moved through the supply chain in a container (e.g., pallets, cases, totes, etc.). It allows the container to remain intact (un-opened) so as not to undermine tamper-evident security features. It also helps maintain cost-effective material handling.

Trading partners utilize other information such as shipping documentation, physical inspections and existing trading partner relationships as part of the inference practice today. If there is a positive correlation and the integrity of the container has not been compromised, all items within the container may be accepted as being present.

With regard to serializing primary and secondary packaging, meeting existing statutory requirements demands that the integrity of serial numbers be maintained as drug products are moved across the supply chain. As with a non-serialized product, it is essential to protect the integrity of outer packaging as the product moves through the supply chain.

Hence, the essential topic for this document is “the practice of inference.” This document and its recommendations may provide a useful starting point for other segments of the healthcare supply chain (e.g., medical devices).

The Principle of Inference

As part of the discussion, *inference* has become a topic of interest for the pharmaceutical supply chain community. *Inference* is a mechanism that enables supply chain partners to leverage strong supply chain practices to meet the potential challenges associated with the receiving/shipping of serialized items.

Inference applies in instances where a collection is moved through the supply chain in an outer container (e.g., pallets, cases, totes, etc.), and less than 100% of data carriers in that collection are read by recipients. In such circumstances, inference enables the recipient of the collection to leave the outer container intact. In order to validate receipt of the entire collection, the recipient reads the serialized identifiers for the visible items, cross-checks them with the shipping documents for the collection and outer container bundle, and verifies the integrity of the outer container bundle and its security features. If all three conditions are confirmed, the rest of the items in the collection can be inferred to be present.
Opening containers, particularly cases, as items travel through the supply chain raises serious concerns. It is not only time-consuming and costly, but it also introduces new risks. Open cases are vulnerable to tampering, theft and product mix-up. Moreover, many manufacturers today use tamper evident tape or seals to ensure the integrity of cases, and such cases remain sealed until items are staged for picking operations. Opening sealed cases would negate the effectiveness of any such security feature.

Inference can be used under the following conditions:

- A collection is present (e.g., case, tote, pallet, etc.).
- The collection is identified with a unique serial number, and each item in the collection is also identified with a unique serial number.
- The hierarchical relationship of all serial numbers associated with the collection (“the aggregation”) is recorded as the collection is built (e.g., serial number of the pallet, serial numbers of all cases on the pallet, serial numbers of all items in each case on the pallet, etc.).
- The receiving supply chain partner receives an electronic communication detailing the aggregation of the collection (i.e., the serialized numbers and the hierarchical relationship of those serialized numbers within the collection).
- The receiving supply chain partner has assurance that the integrity of the collection has remained intact since leaving the last supply chain partner and can confirm that the integrity of the collection has not been compromised.

Inference concludes when the outer container is opened and the serialized identifier for each item in the outer container is physically available to be read.
Inference as an Applied Concept

Supply chain inference is not a new concept. In fact, it is used extensively in retail and other industries where full cases are not routinely opened at the point of receipt. Rather, the receiver uses visual inspection, supporting documentation, and existing supply chain partner relationships demonstrating shipping accuracy and integrity to validate receipts. For example, the identity of a barcoded unit that is packed in a sealed case can be inferred based on supporting evidence such as:

- No signs of tampering
- Clean bill of freight
- Delivery consistent with expectations (day, time, etc.)
- Standard case count
- Match across outer container serial number, purchase order, advance shipping notice, shipping documentation, and visual inspection
- Existing history with the supply chain partner

Inference is also commonly used in the pharmaceutical supply chain today – often for safety and security reasons. For example, many customers prefer to leave manufacturer security features like seals or tamper evident tape intact in order to decrease risk of tampering or loss. Moreover, some customers require manufacturer unopened cases to ensure package integrity. In these situations, inference is a practical necessity. The use of inference is also common for other types of packaging that are routinely left intact (e.g., bundle of 10 count syringes, etc.). In all of these examples, supply chain partners using inference would rely on their existing processes for resolution of shortages and other exceptions.

Applying Serialized Inference to Pharmaceuticals in the Supply Chain

Within the context of the U.S. pharmaceutical supply chain, serialized inference is defined as the process a supply chain partner could use to facilitate safety and efficiency in the receiving of items without physically reading each serialized identifier at the time of receipt. The identity of serialized items can be inferred based on information provided by the up-stream supply chain, reasonable inspection of the product, and application of Serialized Inference Processes by both the shipping and receiving partners. Serialized Inference Processes define the specific actions that should be completed within aggregation, shipping and receiving processes in order to support the use of inference in the supply chain. In order to use inference for pharmaceuticals and pedigree, Serialized Inference Processes should be defined for each packaging unit (e.g., pallet, case, tote, etc.) for all aggregation, shipping and receiving processes.
For example, Table 1 presents Serialized Inference Processes that detail the steps recommended for inclusion in aggregation processes in order to facilitate the use of inference:

<table>
<thead>
<tr>
<th>Table 1: Serialized Inference Processes for Aggregation Processes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Single item commission</strong></td>
</tr>
<tr>
<td><strong>Item to case aggregation</strong></td>
</tr>
<tr>
<td><strong>Case to pallet aggregation</strong></td>
</tr>
<tr>
<td><strong>Tote, mixed case or overpack aggregation</strong></td>
</tr>
<tr>
<td><strong>Mixed pallet aggregation</strong></td>
</tr>
</tbody>
</table>

In contrast to the Serialized Inference Processes for aggregation shown above that deal primarily with tagging and information collection, Serialized Inference Processes for shipments and receipts deal primarily with reading and inferring tags and identifiers. It should be noted that Serialized Inference Processes for shipments and receipts assume the hierarchy and packaging integrity remain intact from the Commission/Aggregation process.
Inference in Action in the Pharmaceutical Supply Chain

Using the *Serialized Inference Processes* described above, supply chain partners can use inference as a method for ensuring that there is enough evidence to certify receipt of serialized items without physically reading each unique identifier. The inference process from manufacturer to wholesaler to pharmacy is demonstrated below in a chain of custody model representing the shipping and receiving of a manufacturer sealed case of pharmaceuticals.

The following example is intended for use with homogeneous cases, but does not preclude the use of inference in other situations. The example also does not cover exception processing.

### Manufacturer

**Step 1.** All identifiers of bottles are scanned as they are packed into a case. (In the case of RFID, the items may be scanned or read after they are packed.)

**Step 2.** A case identifier is created and scanned, and the case/bottle identifiers are associated with one another within the manufacturer’s system.

**Step 3.** The case is put away.

**Step 4.** Upon shipping the case to a supply chain partner, the manufacturer “infers” that the previously identified bottles are in the case, and creates the appropriate electronic shipping documents based on that information.

**Step 5.** Electronic shipping documents are sent to the wholesaler.

### Rationale for Inference:

- The case remains in the control of the company.
- Product movement practices are documented and used (for example, a company’s own processes, Good Manufacturing Practices (GMP), good distribution practices, etc.).
- The site is physically secure.
- The case is visually intact.
- The previously gathered information from product movements are retained.
Improving Patient Safety and Supply Chain Efficiency

**Wholesaler**

Step 1. The wholesaler receives the electronic shipping documents.

Step 2. The product arrives at the wholesaler.

Step 3. The wholesaler visually confirms the integrity of the shipped case or pallet.

Step 4. Product is inferred based on electronic shipping documents that match the shipped case or pallet, security features and integrity of the container are intact.

Step 5. The case is put away.

Step 6. When shipping the full sealed case to a supply chain partner, the wholesaler “infers” that the packages identified in the manufacturer’s shipping documents are in the case, and creates the appropriate electronic shipping documents based on that information.

Step 7. The wholesaler’s electronic shipping documents are sent to the pharmacy distribution center.

**Pharmacy Distribution Center**

Step 1. The pharmacy distribution center receives the electronic shipping documents.

Step 2. The product arrives at the pharmacy distribution center.

Step 3. The pharmacy distribution center visually confirms the integrity of the shipped case or pallet.

Step 4. Product is inferred at the point of receipt based on electronic shipping documents that match the shipped case or pallet.

Step 5. The case is put away.

Step 6. The case is opened for picking.

Step 7. Items are picked from the case, read and matched against the wholesaler electronic shipping documentation effectively concluding inference.

Step 8. The pharmacy distribution center creates and sends shipping documents to the pharmacy.
Pharmacy (wholesaler ships direct to pharmacy)

Step 1. The pharmacy receives the electronic shipping documents.
Step 2. The product arrives at the pharmacy.
Step 3. The pharmacy visually confirms the integrity of the shipped case or pallet.
Step 4. Product is inferred at the point of receipt based on electronic shipping documents that match the shipped case.
Step 5. The case is put away.
Step 6. The case is opened for stocking.
Step 7. Inference can conclude when the case is opened and the serialized identifier for each item in the case are physically available to be read.

The Decision to Use Inference

The use of inference remains an individual company decision. In deciding whether to use inference for items moving through the supply chain and/or internal processes, a company will build an internal case for inference that can be thought of as building layers of trust. Each layer reinforces confidence in the use of inference, and strengthens the case that items for which receipt was inferred were actually received.

There are four factors that can be considered when deciding whether to use inference: Trusted Relationships; Best Practices; Corroborative Information; and Physical Security. Some of the qualifications to be considered for each factor are presented below. These can be used when building the case for a company’s decision to use inference.

Supply Chain Partner Relationships

The relationship between supply chain partners can impact the decision about whether to use inference to a great degree. The level of trust in supply chain partner relationships can be established using a number of indicators including:

- Agreements
- Audit results
- Documented practices of the supply chain partner
- Past performance as measured by the historical accuracy of received documentation (e.g., advance ship notice, pedigree, bills of lading, etc.), shipment condition (e.g., intact, sealed cases) and accuracy of received bundles
Good business practices, both a company’s and its supply chain partners, contribute to a secure supply chain (e.g., good manufacturing practices; good distribution practices; good pharmacy practices; etc.). The level of trust in business practices can be established using a number of indicators like:

- Supply Chain Partner Scorecarding
- Performance Auditing Process
- Documented controls and Standard Operating Procedures
- Routine capture of quality metrics to minimize “defects” of inbound and outbound product
- Implementation of process changes whenever process errors are detected in order to prevent future errors
- Periodic review of processes for improvement opportunities

In addition, when a company uses inference practices, its supply chain partners may require additional documentation, assurances about the use of best practices, and/or proof of physical security.

**Corroborative Information:**

Documentation and observations for the particular items under consideration also inform a decision about whether inference would be appropriate. Various types and sources of corroborative information can be used, including:

- Physical inspection showing:
  - Original manufacturer tape intact
  - No signs of tampering
  - Clean bill of freight
  - Complete pedigree trail
  - Confirmation of outer packaging identification against supporting documentation
- Transit time consistent with expectations
- Authentication capability (i.e., direct supply chain partner verification, repositories or services where supply chain partners can verify serial numbers)
- Electronic documents such as:
  - EPCIS ship and receive information
  - Pedigrees
  - Advance Ship Notices
  - Bills of Lading
Physical Security

Documented security policies and procedures within physical plants, distribution centers and facilities contribute to establishing the trust to support the decision to use inference. Likewise, documented security policies and procedures for transport vehicles are an important consideration as well.

The practice of inferring the contents of packaging based on secure corroborative information, best practices, trusted supply chain partner relationships and physical security is thought to be an appropriate means to provide the appropriate level of security and efficiency within the supply chain.

Ultimately, each company must consider all of this information in the context of the prevailing regulatory environment under which the inference step is proposed and the company’s own risk threshold.
Appendix: References & Recommended Reading

- GS1 Healthcare US Website
  http://www.gs1us.org/healthcare

- GS1 Healthcare US Document Library
  http://www.gs1us.org/hclibrary

- Industry Announcements
  http://www.gs1us.org/library?EntryId=344

- GS1 Healthcare US Web Seminars
  http://www.gs1us.org/hcedu

- GS1 US Glossary
  http://www.gs1us.org/glossary

- GS1 US Product Catalog

  GS1 US offers a comprehensive line of technical implementation guidelines for GS1 Standards.
  http://www.gs1us.org/productcatalog
Disclaimer

GS1 US, Inc.™ is providing this document as a service to interested industries. This document was developed through a consensus process of interested parties.

Although efforts have been made to assure that this document is correct, reliable, and technically accurate, GS1 US MAKES NO WARRANTY, EXPRESS OR IMPLIED, THAT THIS DOCUMENT IS CORRECT, WILL NOT REQUIRE MODIFICATION AS EXPERIENCE AND TECHNOLOGICAL ADVANCES DICTATE, OR WILL BE SUITABLE FOR ANY PURPOSE OR WORKABLE IN ANY APPLICATION, OR OTHERWISE. Each user of this document assumes all risk and responsibility for its use of the materials.

Use of this document is with the understanding that GS1 US accepts no liability whatsoever for any direct, indirect, special or other consequential damages of whatever kind resulting from whatever cause through the use of the document or any information therein, even if GS1 US has been advised of the possibility of such damages.