



Background and Introduction

MTS Medication Technologies (MTS) is pleased to submit comments to the Food and Drug Administration (FDA) regarding Docket No. 2005D-0174, *Draft Guidance on Expiration Dating of Unit-Dose Repackaged Drugs; Availability*. MTS is a manufacturer of proprietary packaging equipment and unit dose materials (punch cards) primarily used by pharmacies to individually repackage medications for use by residents of long-term care facilities and other individuals who require unique medication packaging and distribution systems. In a more limited capacity, MTS also provides unit dose packaging materials to FDA-licensed repackagers.

Through these comments, MTS:

- Provides background information and certain practices related to prescription medication repackaged by a pharmacy provider MTS understands that this draft guidance covers only FDA-licensed repackagers. However, MTS provides background information for the record to show that future changes in federal and state laws and regulations might be adopted by other agencies that govern the practice of pharmacy. This could affect the ability of pharmacies to meet the packaging needs of patients in long-term care and other alternate care settings.
- Provides an overview of the existing United States Pharmacopoeia (USP) Standards for Product Dating (beyond-use date). These comments will also consider the differences and potential confusion that could occur among state pharmacy regulations, USP Standards, and the FDA guidance document. Please refer to the attached memorandum to the USP dated April 26, 2001 regarding Beyond-Use Dating Guidelines.
- Provides an overview of the complexities and costs of producing thermoformed plastics, with high barrier characteristics, by converters like MTS.
- Seeks FDA clarification regarding this draft guidance and the flexibility of the FDA to consider a broader range than Class A to achieve twelve-month dating and understand the applicability under the new guidance of current Class B standards, which currently allow a six-month expiration dating.

Overview of MTS and Other Converters' Products and Plastics Commonly Used for Packaging by Pharmacies and Repackagers

MTS is a converter of packaging materials used primarily by long-term care pharmacies and some drug repackagers for repackaging medications into 30-, 60-, or 90-dose blister cards (colloquially known as punch cards, bingo cards or blister packs). MTS' processes use flexographic printing presses that heat, seal, coat and print on 20 point SBS virgin cardboard, die cut the appropriate blister format and laminate foil to one-half of a fold-over card. Blisters are manufactured out of either PVC or PETG plastic in 6 and 7.5 mill gauges and produced on wide-web thermoformers, which preheat, form and die cut in process.

As stated above, MTS and its competitors utilize PVC or PETG plastic. There are also several pouch type systems on the market that utilize materials ranging from low-grade polyethylene to cellophane.

However, MTS estimates this type of equipment services less than 5% of the long-term care pharmacy market.

MTS presently supplies products that meet current USP Class B standards. MTS has also been working on new products that may meet Class A specifications. However, these products are in the early stages of testing. MTS believes it is 12 to 18 months away from being able to produce these new flexible films in mass production in order to be able to meet industry demands.

Overview of Packaging Systems for Pharmacies that Service Long-Term Care Facilities

MTS products are primarily used by long-term care pharmacies that place patient-specific medications into a variety of packaging systems, including punch cards. MTS led the industry in automating the ability to package into punch cards and has developed a full range of equipment from automated heat sealers to fully automated fill and seal machines that dispense patient specific labeled medications on a just-in-time basis. These machines are also designed and manufactured by MTS and sold to long-term care pharmacies. The primary end users of these pharmaceutical products packaged by long-term care pharmacies are nursing home and assisted living facility residents.

Unit dose/punch card packaging products are an industry standard in long-term care facilities that generally do not have pharmacies within their walls; therefore, they contract with the long-term care pharmacy providers for pharmaceutical dispensing, packaging and clinical services. Federal standards require that nursing facilities must meet stringent Medicare and Medicaid conditions of participation and must establish an organized medication distribution system. Most of the 15,000 Medicare- and Medicaid-certified nursing facilities use punch card packaging systems by MTS and other manufacturers to meet this standard. Other long-term care facilities, including assisted living, continuing care retirement communities, and state regulated facilities, often elect to use punch card packaging systems because of the benefits it provides for compliance and efficiency in administration. Punch card packaging systems are likely to become more popular in the future as the federal government and other pharmacy payors recognize its value in improving medication adherence.

MTS understands that the current federal and state regulatory framework clearly distinguishes the activities of long-term care pharmacies from drug repackagers. Long-term care pharmacies operate under Board of Pharmacy rules and licenses; however, some activities associated with packaging medications for use in long-term care facilities are similar to the functions of a repackager. MTS believes that recognition of this distinction is important now because potential adoption of the FDA changes by other regulatory entities could have unintended consequences on laws and regulations affecting pharmacies. If long-term care pharmacies were required to meet Class A standards today, they would be unable to meet the medication needs of patients that they presently service. This is a function of cost as well as the inability of converters like MTS to be able to meet the immediate need of the pharmacies.

Potential confusion between various standards and regulations that might occur.

USP recognized the packaging activities of long-term care pharmacies and enacted guidelines, adopted by most state Boards of Pharmacy, to ensure the quality of patient-specific, unit dose packaged medications provided by pharmacies. Generally state regulations refer specifically to the USP standards or spell out requirements based on the USP standards. Until USP issued new standards in the year 2000, USP and the FDA utilized the same guidelines for beyond-use dating, which designated classes of packaging from “A” through “D”. These USP standards for pharmacies allowed placement of a six-month beyond-use dating on packages that met the Class B specifications provided that the six months did not exceed 25% of the current expiration date on the manufactured bulk container. Certain other criteria also existed.

Then, in the year 2000, USP revised its beyond-use dating guidance to allow a twelve-month expiration date when using material considered “better than PVC.” The USP never defined “better than PVC” and therefore, there has been much confusion and inconsistency in the application of the beyond use guideline.

Manufacturing complexities associated with high barrier plastics.

MTS is concerned that if pharmacies are required to use materials considered better than PVC, the functionality and practicability of blister cards may decrease and thus lead to potential for problems in the packaging process. Pharmacies that package individual patient medication use pre-formed blisters made from PVC or PETG plastic that must be stacked together and boxed for shipment for use by pharmacies at a later time. Because none of the pharmaceutical companies nor repackagers utilizes pre-formed blisters, they do not have the necessity to de-nest stacked blisters. Therefore, the plastic manufacturers have not applied release agents, such as silicone coatings to enable these blisters to be separated. From a production standpoint, this creates substantial problems in either the operator’s manual de-nesting of these blisters or the automated pick-and-place mechanisms that are used to de-nest these blisters for automated equipment. Because pharmaceutical companies do not include silicone as an agent in their NDAs, the plastic manufacturers are prohibited from introducing the substance into their facilities at this time. MTS has not been able to identify a manufacturer of PVDC or Aclar¹ willing to introduce coatings or other release agents into their operations. Secondly, these plastics are much more expensive than those presently utilized. MTS estimates it would cost long-term care pharmacies \$37 million annually to convert to an Aclar blister to meet Class A standards. MTS believes these costs are unnecessary to provide a higher barrier product. MTS has moisture and permeation data showing that our packaging meets current Class B standards and new materials ranging from 1 mg per day to a Class A standard. MTS would be happy to share this information upon request.

MTS Recommendation to FDA

- In the event that State Boards of Pharmacy or the United States Pharmacopoeia adopt the new FDA guidelines, MTS recommends that the FDA also continue the use of the current Class B standard allowing for six-month expiration dating.
- MTS would urge the FDA to consider a broader standard than .5 mg per day in order to allow the use of a twelve-month expiration dating. MTS believes that it can more easily meet the markets demand with a higher barrier product if the standard were 1 mg per day. This would still be a 400% improvement over the current Class B standard, which allows up to 5 mg per day.

MTS suggests that FDA review MTS stability data before it makes a final recommendation. This data will show that higher permeability standards can be met without utilizing more expensive Class A packaging. MTS can provide this information to FDA in a blinded manner separate from these comments.

MTS thanks the FDA for the opportunity to provide comments on the draft guidance, and MTS will be happy to follow-up if the FDA seeks further data or clarification. You may contact me at 727-576-6311.

Sincerely,



Todd Siegel
President & C.E.O.

¹ Aclar® is a registered trademark of Allied Signal, Inc.