

Detection and Link Analysis of Counterfeit Altuzan® Printing Defects Using Light Microscopy and Digital Imaging

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In 2012, counterfeits of Roche's oncology medication Altuzan[®], a foreign version of the U.S. Food and Drug Administration (FDA) approved medication Avastin[®], were detected in the U.S. drug supply (**FIG 1**). Their emergence was due to medical practices in the U.S. purchasing this unapproved product from foreign sources at discount prices, thereby circumventing the secure supply chain [1]. Chemical testing at the Forensic Chemistry Center (FCC) revealed that some of the counterfeits contained no active ingredients, and were contaminated with mold and bacteria [2]. Due to the public health emergency, it became crucial to identify the counterfeits in circulation, to determine if they had come from a common source, and to remove them from the drug supply.

Stereoscopic light microscopes (SLM) and digital imaging equipment (DIE) were used to compare the packaging and the printing processes observed on the counterfeits to printing processes used on authentic Altuzan[®]. Using SLM and DIE, it was determined that the graphics, lot numbers, and expiration dates on the counterfeit cartons and vial labels were printed using poor quality offset lithography, which was not consistent with authentic packaging. Offset lithography is commonly used by counterfeiters due to its relatively cheap cost and versatility [3]. It is characterized by a clean, even distribution of ink from the center to the edges of the print area (**FIG 2A**). Authentic vial labels are printed using an entirely different printing process that is characterized as a dark ring or halo around the print area (**FIG 2B**). The detection of these types of printing processes is a rapid technique that can be used to screen through large volumes of samples quickly to identify the counterfeits.

Unlike authentic manufacturers that have strict regulations for lot number traceability, counterfeiters commonly use the same printing process to print the graphics and the lot numbers/expiration dates on counterfeit packaging. This practice provides for quick isolation of the counterfeits for further chemical analysis, which eliminates the need to analyze thousands of unapproved authentic products. When the counterfeit lot number becomes known by authorities, the counterfeiter may change the lot number while occasionally reusing one or more of the same printing plates from the old counterfeit. The same defects that may be present on the old counterfeit printing plates are then transferred to the new counterfeit packaging (**FIG 3**). These microscopic defects provide a fingerprint for a particular counterfeit that can be used to link counterfeits to a common source even if the lot numbers are changed. The linking of counterfeits to a common source can assist the investigators in determining how many possible sources of the counterfeits exist and where in the supply chain they were introduced. The individuals responsible for illegally selling Altuzan[®] into the U.S. market, and thereby introducing the counterfeit Altuzan[®], were arrested. They entered guilty pleas, and were sentenced to 27 and 30 months in prison [4].

- [1] www.fda.gov/Drugs/DrugSafety/DrugIntegrityandSupplyChainSecurity/ucm298047.htm
 [2] www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm298583.htm
 [3] A. Lanzarotta, *et al*, “Analysis of Counterfeit FDA-Regulated Products at the Forensic Chemistry Center: Rapid Visual and Chemical Screening Procedures Inside and Outside the Laboratory”. *American Pharmaceutical Review*, April 2015, p. 27.
 [4] www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm431343.htm

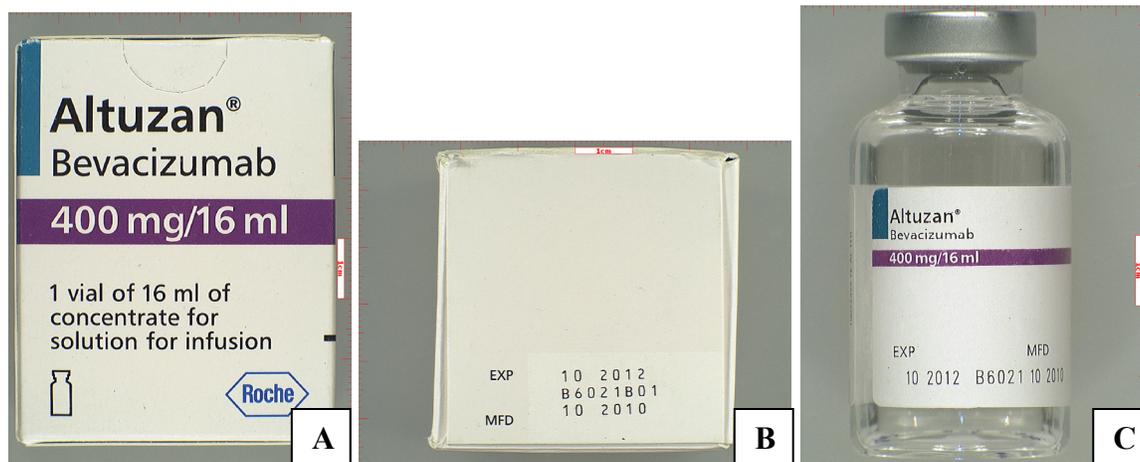


Figure 1. Counterfeit Altuzan® carton (A), carton lot/expiration (B), vial/vial label (C).

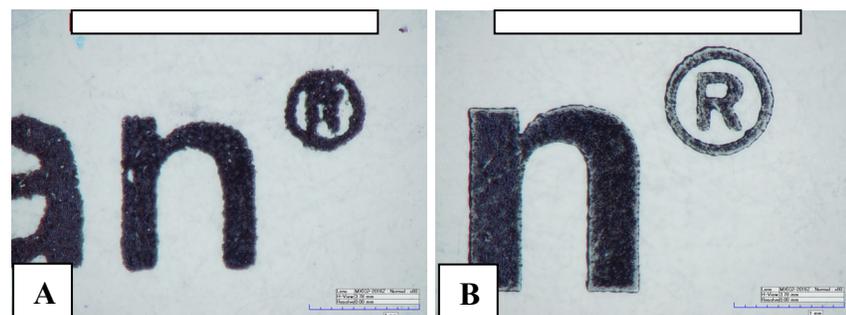


Figure 2. Counterfeit vial label (A) printed using offset lithography compared to authentic (B).

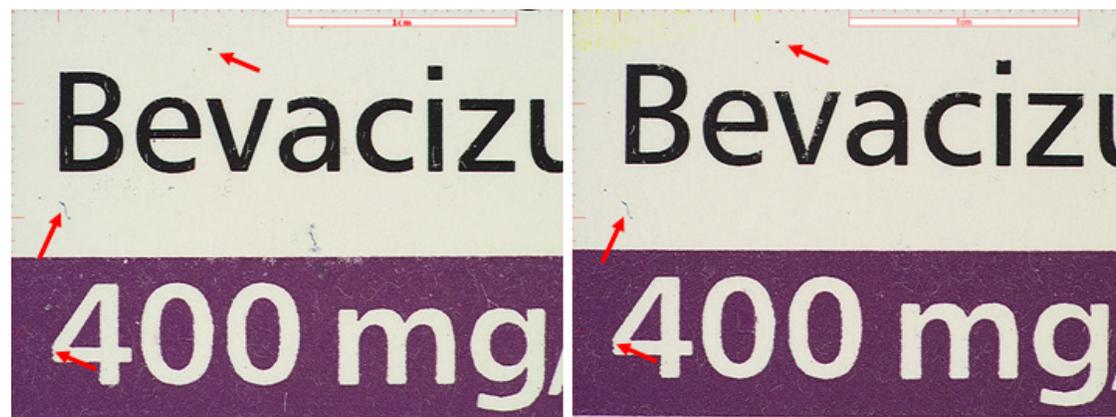


Figure 3. Counterfeit Altuzan® cartons from two different lot numbers showing consistent printing defects (red arrows) linking the counterfeits to a common source.