

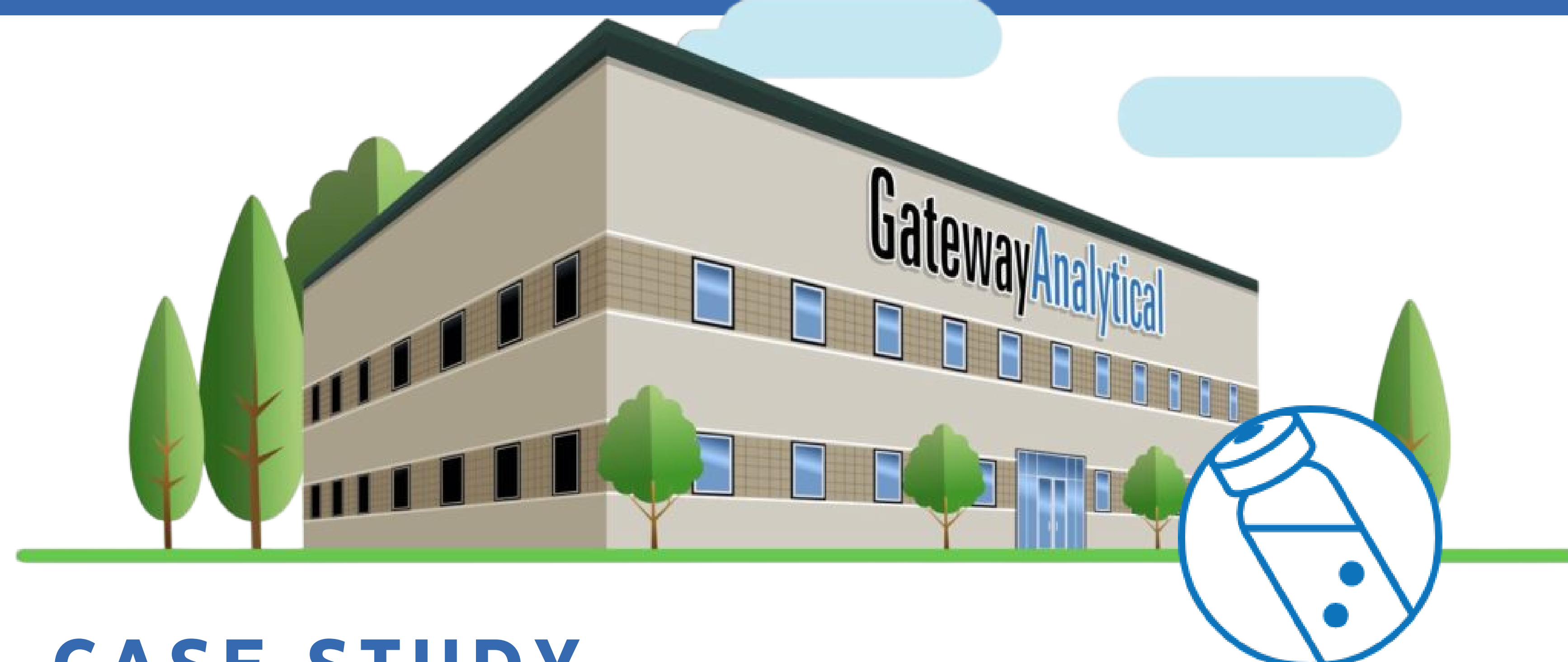


CLIENT GOALS:

A biopharmaceutical manufacturing company needed to determine the source of cellulose fibers that continued to be present in their manufactured drug products. This contamination was a frequent occurrence and happened with each manufacturing run, so the client was eager to determine the source.

KEY OUTCOMES:

- + Thorough identification and characterization of the foreign contaminants
- + Comprehensive reference material list of possible sources of cellulose fiber contamination
- + Independent third-party laboratory screening to rule in/out possible sources of the contamination
- + Multi-analytical testing methods to determine similarity of fibers which can be strikingly similar in appearance
- + Comprehensive report detailing the laboratory steps and methods for determining possible sources of the fiber contamination



CASE STUDY FOREIGN PARTICULATE MATTER

EXECUTIVE SUMMARY

Foreign particulate matter contamination is a common occurrence in pharmaceutical manufacturing, especially for injectable drug products. Among the many foreign particles that present themselves in a pharmaceutical manufacturing environment, small fibers composed of cellulose are quite common. Determining the source of fibers that are so common to the environment can present challenges to laboratories who are not equipped to perform such testing.

A biopharmaceutical company continued to have particulate matter issues related to cellulosic fiber contamination in their filled vials. This contamination was not specific to any manufacturing run; it seemed to occur frequently with each different batch. After several investigations that determined the fibers to be composed of cellulose, the client was ready to begin looking for the source of the contamination.

Gateway Analytical's expertise is the source determination of foreign and unknown particulate matter in injectable drug products. Gateway requested that the client submit many of the common materials used in their manufacturing process as references. Gateway then used a top-down approach to associate or rule out these reference materials based on their macro- and microscopic characteristics. Further testing and analysis determined how similar or dissimilar the reference materials were to the cellulose fiber contaminants.

Gateway Analytical concluded the investigation by providing a detailed report which summarized the screening and testing. Gateway narrowed the source to five possible materials that could be contributing to the contamination. The client proceeded to either exchange these materials for different materials or use the materials in more effective ways to help reduce future contamination.

THE CHALLENGES

The client had previously submitted samples to another laboratory for identification of the fiber contaminants. This laboratory only provided photographs and single-method testing to determine that the fibers were composed of cellulose. Frequent testing re-confirmed the presence of cellulose, but provided no further characterization or suggestions for reducing its occurrence.

The client frequently rejected multiple drug product units with every manufacturing run. In some cases, the client was required to notify their sponsoring client to inform them about the fiber contamination. The client was not able to provide their client with a conclusion as to why or where the fiber contaminations were occurring.

OUR APPROACH

Gateway Analytical first performed a thorough characterization of the foreign particulates — in this case, the cellulose fibers. Macro- and microscopic characteristics were observed and noted as part of the testing. Optical imaging provided photo-documentation for the number, size and occurrence of the fibers once isolated from the vials. Particle-sized images of the fibers were collected for documentation of their size and appearance.

Multi-analytical methods were employed to make a thorough characterization of the fibers. This aided in the source determination steps to determine how similar or dissimilar the contaminating fibers were from the reference materials of the manufacturing environment.

Reference materials were requested from the client. Gateway Analytical used macro- and microscopic methods to first determine the similarity of the reference materials to the fiber contaminants.

Next, Gateway Analytical ruled out reference materials as sources and identified those materials which required further characterization to determine if they were a possible source. The same multi-analytical methods were used to characterize the reference materials. Gateway Analytical determined which reference materials could be possible sources based on their similarity by means of conclusions supported with multi-analytical methods.

A comprehensive final report was submitted to the client which detailed the rationale for which reference materials could and could not be a source of the fiber contamination.

**INDUSTRY LEADING
TURNAROUND TIME**

**MULTI-DISCIPLINED
ANALYTICAL EXPERTS**

**FULLY CERTIFIED &
ACCREDITED LAB**

**PERSONALIZED
CUSTOMER SERVICE**

Turnaround Times: Standard: 4-5 Days Expedited: 3 Days Rush: 24 Hours

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