Forensic-Grade Products for Human Identification: Preparing for ISO 18385 Requirements

Promega Corporation
Contact us: genetic@promega.com

Currently, Promega meets or exceeds the guidelines put forth by ENFSI, SWGDAM and BSAG to minimize the risk of human-to-product contamination.

This White Paper outlines the manufacturing standards for Promega Genetic Identity products, and summarizes our preparation for compliance with the ISO 18385 Standard.

The Problem of DNA Contamination

The effects of DNA contamination can be especially problematic in forensic analysis. The introduction of foreign DNA to a crime scene sample, either at the scene itself or during laboratory analysis, can have devastating effects on an investigation—from rendering a single sample useless to compromising an entire investigation.

Consumables used at a crime scene or during subsequent laboratory analysis are one potential source of such DNA contamination. One prominent example of this is the case of the "Phantom of Heilbronn", where DNA recovered at over 40 crime scenes from 1993-2009, and thought to be that of the perpetrator, was eventually found to have been introduced to each scene via the cotton swabs used for sample collection. This case highlights the importance of ensuring that reagents, sample collection devices and plasticware used at crime scenes or during laboratory analysis are manufactured to a standard that minimizes the risk of DNA contamination.

The ISO 18385 Standard

In 2009, the European Network of Forensic Science Institutes (ENFSI), the Scientific Working Group on DNA Analysis Methods (SWGDAM) and the Biology Specialist Advisory Group (BSAG) published a position statement requesting that manufacturers of disposable plasticware and other reagents for the forensic market take additional precautions to prevent contamination in their manufacturing processes (1). This position statement has been used by the international forensic community as a basis for drafting ISO 18385, "Minimizing the risk of DNA contamination in products used to collect and analyze biological material for forensic purposes". This draft is currently under review by participating ISO member countries.

The ISO 18385 Standard is expected to provide manufacturing requirements for forensic-grade products, and specify acceptable methods and pass/fail criteria for DNA contamination testing.

Current Promega Manufacturing Standards

Once the ISO 18385 Standard is published, manufacturers who comply can label Human Identification products as Forensic-Grade. This paper outlines our preparation for compliance with ISO 18385, once the standard is published. Today, Promega manufacturing processes meet or exceed the guidelines proposed by ENFSI, SWGDAM and BSAG to minimize the risk of human-to-product contamination.

- We maintain a robust Quality System, having obtained ISO 9001-certification in 1998. In addition, our manufacturing facilities in Madison, Wisconsin have been ISO 13485-certified since 2006 to meet the requirements of our medical device and in vitro diagnostics customers.
- We have manufacturing capabilities and facilities specifically designed for Genetic Identity products.
- We are participating in the development of, and are evaluating our manufacturing processes for alignment with, ISO 18385 draft requirements.

Manufacturing Capabilities for Genetic Identity Products

In addition to the quality standards required for compliance with our quality system, Promega Genetic Identity products are manufactured in dedicated manufacturing suites designed to minimize the risk of product-to-product and human-to-product contamination. All short tandem repeat (STR) products for forensic analysis are QC tested to ensure performance.

- ***Specialized Staff for Forensic Products***. All Promega employees involved in the production of Genetic Identity products participate in continuous training to maintain a high level of expertise and skill. We control key raw materials from component manufacture through bulk reagent production, including synthesis of the oligonucleotides and proprietary dyes used in our Genetic Identity products.
- ***Separation of Manufacturing Spaces for Pre- and Post-Amplification Components***. We understand the importance of separating pre- and post-amplification processes to protect our products and our customers. We have robust manufacturing and dispensing processes written into our Standard Operating Procedures to reduce the risk of contamination between pre- and post-amplification STR kit components. Only trained personnel are allowed to enter pre-amplification manufacturing suites, and those personnel are required to wear lab coats, safety glasses, hairnets, face masks, beard covers (if applicable) and gloves at all times. Pre-amplification suites are dedicated to the manufacture of different pre-amplification reagents. Separate manufacturing suites are used for: 1) Manufacture of buffers, master mixes and amplification-grade water; 2) Manufacture of primer pairs; and 3) Manufacture and QC testing of control DNA for STR systems.

All Promega employees involved in the production of Genetic Identity products participate in continuous training to maintain a high level of expertise and skill.

- ***Quality Control of Bulk and Manufactured Materials.*** Products are controlled and tested at key steps throughout manufacture: 1) Incoming critical raw materials are evaluated to ensure that they meet our quality requirements; 2) Intermediate manufactured products are QC tested, and reviewed and released by QA prior to use in bulk manufacturing; 3) Bulk manufactured products are QC tested and QA released prior to use in finished kits; and 4) Finished products (STR and qPCR kits) are QC tested and QA released prior to sale.
- ***Minimizing Human-to-Product Contact and Product-to-Product Contamination.*** Contact between manufacturing staff and product is minimized in several ways: 1) Gowns, masks, hairnets and gloves are required; 2) Critical reagents are dispensed in environmentally controlled spaces; 3) Where possible, dispensing processes are automated.

  Promega kit packaging staff are specially trained to work with Genetic Identity products. Allelic ladder is packaged in a separate area from other kit components and placed within a heat-sealed, tamper-evident pouch prior to final kit packaging, greatly reducing the risk of product-to-product contamination.

Employee Elimination Database

We maintain an elimination database containing the DNA profiles of all staff involved in the manufacture of Genetic Identity products. The database is anonymous and is searchable upon request.

Searching Promega's employee elimination database can help laboratories who suspect (or need to rule out the possibility) that human DNA from a Promega employee may be present in a product, e.g., when a profile is present in a blank or negative sample. Our highest priority when determining whether we can search a profile submitted by a customer against the Promega employee elimination database is whether we believe we can provide both accurate and meaningful information to the customer.

Promega ISO 18385 Readiness

We are involved, along with other manufacturers, in helping forensic community leaders develop the ISO 18385 requirements. Once ISO 18385 is published, we will take any additional steps necessary to manufacture in alignment with the standard.

In preparation for ISO 18385, we have established a cross-functional team dedicated to the implementation of forensic-grade product manufacturing recommendations. Team involvement across Manufacturing, Quality Assurance, R&D, Marketing and Project Management functions ensures our readiness at an organizational level once the standard is published.

We have performed studies to determine the detection limits for various methods currently used to identify DNA contamination (qPCR and STR analysis), and the sensitivity limits of commonly used detection instruments (2). This study speaks directly to the issues addressed in the draft standard, such as: "What level of DNA contamination is detectable?" and "What is the most appropriate detection method?".

We are currently performing post-production treatment feasibility studies, including evaluation of ethylene oxide gas treatment, for decontamination of plasticware. We are also performing stability studies to ensure that such treatments do not have adverse effects on our products.

Summary

We expect to label Promega Genetic Identity products as Forensic-Grade once ISO 18385 is published and we ensure that we are manufacturing in alignment with the requirements. Promega has produced high-quality products for the forensic market for more than 20 years, and our Genetic Identity kits and reagents are already subject to stringent quality standards at each step in the manufacturing process. We are dedicated to continuing to provide high-quality products for our customers. As a member of the US Technical Advisory Group, we are involved in the development of the ISO 18385 Standard and will continue to work with forensic community leaders to establish and implement quality guidelines.

References

1. Gill, P., *et al.* (2010) Manufacturer contamination of disposable plasticware and other reagents—An agreed position statement by ENFSI, SWGDAM and BSAG. *Forensic Sci. Int. Genet.* **4**, 269–70.

2. Raymond, K., Setlak, J. and Stollberg, C. Examination of Proposed Manufacturing Standards Using Low Template DNA. (2013). [cited: 2014, June, 24]. Available from: http://www.promega.com/resources/profiles-in-dna/2013/examination-of-proposed-manufacturing-standards-using-low-template-dna/

For more information about Promega Genetic Identity products, please contact us at:

genetic@promega.com