A Case Study

Commercial Molecular Quality Controls

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MMQCI
MAINE MOLECULAR
QUALITY CONTROLS, INC.

Scarborough, Maine, US
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Agenda

- Outline of the planning process
  1. The problem and the goal
  2. The analysis
- Results to date
- Your comments

The Process

Observe Problem

↓

Analyze Problem
and
Design a Solution

↓

Test the Solution ⟶ Problem Solved?

Business sells solutions to problems

Goal

Overriding

- Benefit to public health

Laboratory

- Ensure useful test results
  1. Accurate
  2. Affordable
  3. Timely

Analysis

How the laboratory ensures its goal of 99.XX% accuracy.

1. Monitor test system functions that are likely to fail
2. Develop predictive statistics
3. Develop preventive and corrective action guidelines
4. Implement quality system based on these data
   - Levy-Jennings charts, QC rules, etc.
   - Ultimately 6 Sigma or related

Analysis

Statistical definition of test characteristics:

The error rate is known for each mutation and genotype.

Guides usage of the test results.

Used to design testing schemes to achieve a desired medically allowable error rate.

Used to design quality schemes to efficiently ensure a desired performance level.

Six sigma, LEAN

Statistical QC for Genetic Testing: Steep climb – but achievable goal

Analysis

QC materials requirements

1. *Need to monitor all steps in the test process*.
2. *QC needs to monitor all genotypes being tested*
3. *QC needs to yield constant values over time*
4. *QC needs to be easy to manufacture and convenient in use*
5. *QC needs multiple genotypes in one sample*
6. *Rare QC genotypes need to be easily generated*

Synthetic Molecular Quality Control

Solution design

- DNA control sequences are synthesized
- Mutations are created *in vitro*
- Sequences are validated
  ~180,000 bases QS sequenced for 5 CF constructs
- Constructs are stabilized
  >2 yr at 4°C
- Wild type & mutant “alleles” are combined to form genotypes

U.S Patents Issued

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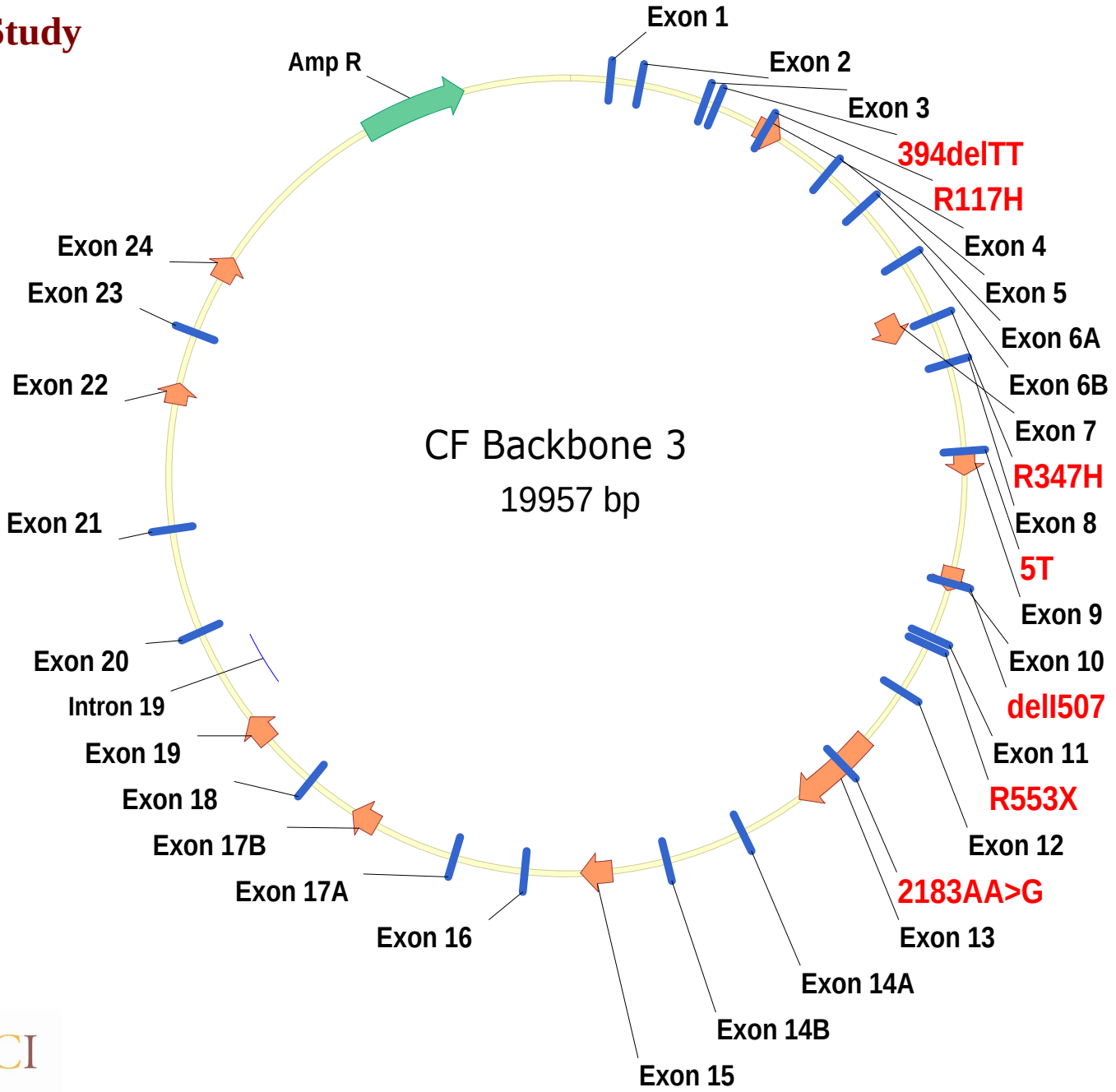

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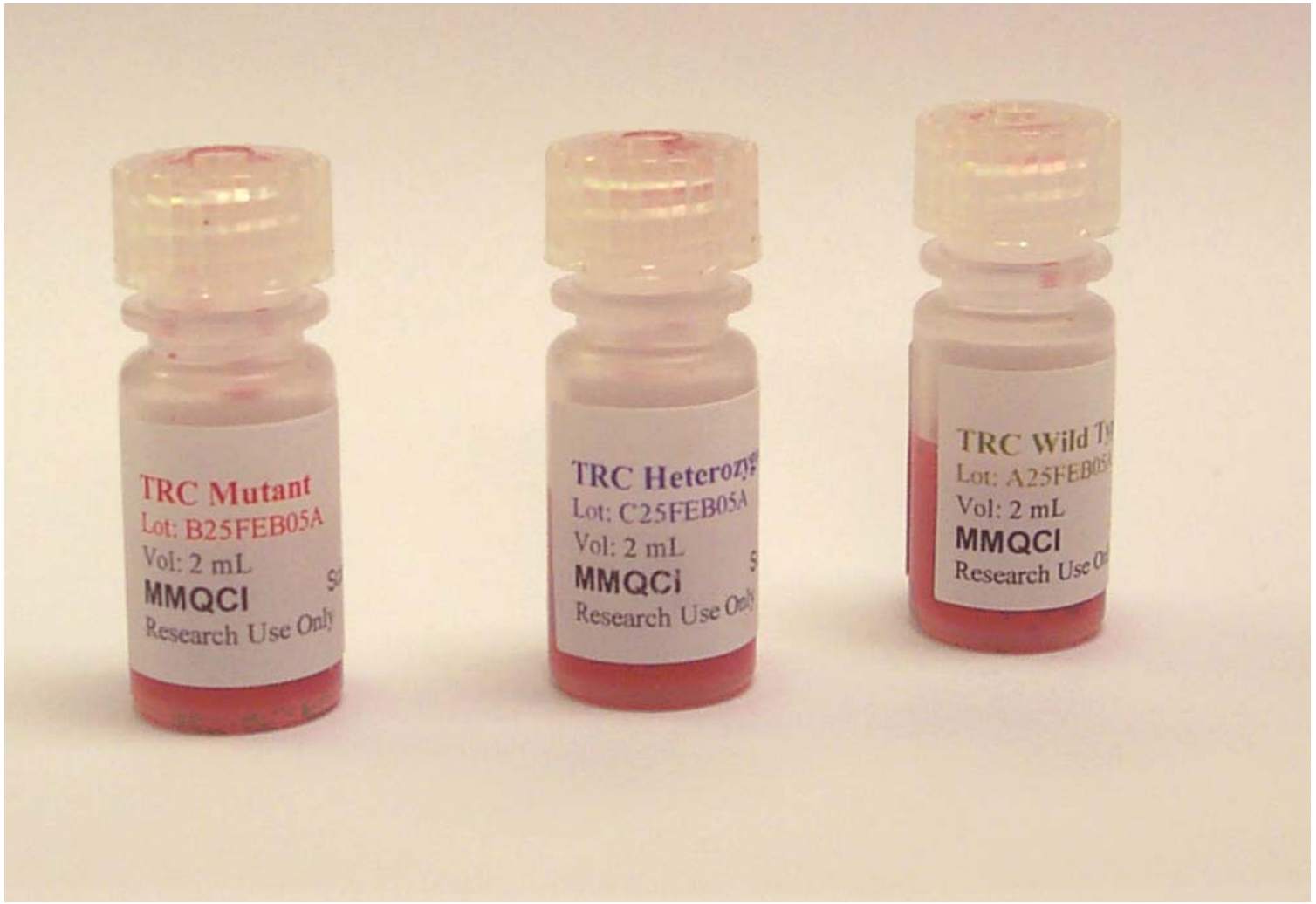

The controls are designed to be extracted and tested in the same manner as whole blood samples.

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Synthetic Control Features

- Precision manufactured.
- Contain all analytes being tested, including rare mutations.
- Affordable and cost effective.
- DNA is extracted. Monitors the entire testing process. "A control material must detect errors in the entire testing process." CLIA Final Rule 2003.
- Stable.
- Traceable.

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Available now:

Cystic Fibrosis	**38 Mutation Control Panel I**
Thrombotic Risk	**FVL, Prothrombin G20210A**
MTHFR	**C677T, A1298C**

Under Development:

Hematologic Translocation Controls

Tuberculosis Control

The Process

Goal: Offer excellent solution(s) to the problem.

Requirement: 1) Fully understand the needs.
2) React quickly to new information.

Questions?

What are the most important outstanding issues?

What would be an ideal solution?

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