Clinical Diagnostic Program
Surrogate Samples Statement of Work

What is the issue?
The speed at which innovative and improved diagnostics are developed can be hampered by the difficulty in obtaining or retaining clinical specimens. This may be due to a variety of reasons, such as rare markers, specimens with markers at the high or low end of the range, specimen stability, the difficulty in obtaining certain specimens due to clinical practice, or patient care takes precedence over the ability to collect specimens under defined conditions. The use of surrogate samples can foster innovation when clinical specimens are difficult to obtain or retain.

What is the goal of this project?
The goal of this project is to establish a foundation under which the use of surrogate samples can support product development with an initial focus on studies to support product submissions.

What will we produce (i.e., Deliverables)?

- **Glossary**
  The Surrogate Samples Work Group will deliver a glossary of terms associated with specimen types including surrogate specimens. The glossary will be developed by assessing currently available terms and definitions found in documents published by national and international agencies as well as standard setting bodies. Whenever possible, currently available and defined terms will be used and where inconsistencies in terms or definitions are found they will be noted. The glossary will provide a standardized vocabulary that will be utilized throughout the other documents developed by the work group.

- **Analysis of Current and Historical Experience**
  The Surrogate Samples Work Group will deliver an analysis of the use of surrogate samples to clearly understand and document under what circumstances such samples might be needed to verify or validate the safety and effectiveness of an IVD medical device. This deliverable will result from the capture of real world examples of when and why developers have used samples other than naturally occurring samples from actual individuals/patients.

  An analysis project plan will be drafted to define and identify the methods that will be used to assess risks and benefits of the use of such samples and sources of data collection. Under consideration is an industry survey, literature review/analysis, analysis of publically available IVD submission data via FDA's

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Premarket Notification and Premarket Approval databases (e.g., 510(k) summaries, SSEs), and internal FDA data provide appropriate resources and IP protections are in place. For the industry survey, MDIC members will be asked to participate and extension to the greater industry is contemplated via engagement with AdvaMed and MDMA. This survey tool will also attempt to capture when and why there have been issues with either the actual development of the sample type or where acceptance of the surrogate sample type has occurred.

Through this approach, the analysis will seek to identify what problems have occurred in the actual work to identify appropriate surrogates and create them, what types of products have been affected, as well as where their applicability has come into question. The gaps so identified will provide input into further development of the framework and points to consider.

- **Framework**
  The Surrogate Samples Work Group will deliver a framework describing when surrogate samples may be used to simulate clinical specimens during the development of in vitro diagnostic tests and to support regulatory submissions for marketing authorization. The framework will be informed by the analysis of current and historical experiences. It will also address scenarios where clinical specimens containing the target analyte are difficult or impractical to obtain. The scope of the document will cover analytical (bench testing) and clinical verification and validation studies. The Framework document will also describe situations where surrogate specimens may not be able to be used if they cannot adequately simulate a clinical specimen.

- **Points-to-Consider Document**
  The Surrogate Samples Work Group will deliver a points-to-consider document. The points to consider document will be an overall summary document that will include elements of the glossary, the analysis and the framework. It is meant to be a formalization of the work of this team that will help guide future decisions on surrogate samples. Through this approach a document will be created that outlines the relevant points to consider when deciding the utility and/or the necessity of using surrogate samples. Elements such as the desired outcome and intention of each study, the clinical prevalence of the desired sample, the technology being explored and the methodology being used will all be considered.

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Who is working on this project?
MDIC has assembled a work group comprised of member organizations and other subject matter experts to guide work on this project.

Industry:
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