Clinical Diagnostics Program
Incremental Improvements Statement of Work

What is the issue?

In vitro diagnostics, or "IVDs," are routinely improved through innovation, resulting in changes to products that make them of greater value to physicians and patients. These changes are often a result of customer feedback or internal company design improvements to increase product reliability or improve manufacturing. Assessment of product changes can require significant data collection, document preparation and delay of implementation due in part to regulatory reviews that may or are perceived to impose significant burdens. The burden must be balanced with the risk to allow modified and/or improved products to reach the market. In some cases, the changes are deemed to have low patient risk or are likely to enhance benefit, but the manufacturer cannot justify because of the difference in perceived risk/benefit between itself and the FDA.

Currently there is not an IVD-specific tool that provides recommendations for determining what kinds and amount of data and documentation are needed to assess safety and effectiveness of modifications and incremental innovations. Such a tool would help align on the goals of industry and FDA to manage changes more efficiently.

What is the goal of this project?

The goal of this project is to establish tools to complement the 510(k) draft guidance.

What are the deliverables of this project?

- **Data Gathering**
  The Incremental Improvements Work Group will gather product change examples. This information will give some further clarity into the types of incremental changes that are being made/not made in the IVD industry. These change examples will follow the change assessment format (Appendix A or B) of the guidance. This information will need to be stated in a way to provide adequate information but not break any confidentiality arrangements.

- **Glossary of Terms**
  The Incremental Improvements Work Group will deliver a glossary of terms associated with incremental changes in *in vitro* diagnostic devices in order to achieve routine improvements, often also referred to as device modifications. 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, such as NIST, CLSI (Harmonized Terminology Database http://htd.clsi.org/), ISO, etc. 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.

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- **Defined change tool with simple rating system (tbd)**
  The incremental improvements group will develop a defined change "tool" with a simple risk-rating system. The tool will be a risk evaluation framework for defining the potential performance effects of single and cumulative product changes to *in vitro* diagnostic tests. The tool will be built by considering many different kinds of design and manufacturing changes to cover the breadth of common, and some not so common, changes that are made to IVDs during their lifecycle.

- **Analysis of and addition of adequate examples in the tool (TBD)**
  Once the change tool is defined based upon examples provided in the data gathering stage and using the expertise within the work group, it will be analyzed/validated by sharing it with a broader group within MDIC for an exercise including adding more examples for each level of change in the tool. Companies will be asked to provide a de-identified change they have already submitted to FDA without providing the result of the review. The description of the change will include the type of product, the type of change and sufficient detail to understand the risk potential. The tool will be applied to see what would be required using this new approach. There will then be the ability to compare the tool result with what was required to actually support the change type in the past. By looking at this comparison across many product types the working group should be able to assess the potential impact of the use of the tool. Once the tool is refined based on this, a broader group of companies will be asked to provide examples for the various types of changes that the tool can address.

- **Examples of appropriate tests/studies or documentation for each change risk level example (D4)**
  The Incremental Improvements Work Group will use the data gathered from the template to deliver summarized examples of changes with enough appropriate technical language to clearly define what tests, studies and documentation are necessary to support incremental improvements. The examples will provide clarity and alignment for industry and FDA when a submission may be necessary to support a change and when it is not. The examples may consist of change categories including raw materials, supplier, manufacturing or performance.

- **Release of Tool**
  The Incremental Improvements Work Group will deliver a Steering Committee approved tool that will be acceptable to FDA and industry. The tool will be accompanied by training aids to ensure full competency with its content. The tool will be shared across multiple delivery platforms (webinar, conferences, and website) in order to reach the broadest industry audience.

- **Conclusion of Project**
  The Incremental Improvements Work Group will review the implementation of the tool after launch to ensure that the FDA and industry users are fully satisfied with its content, language and training. They will also ensure that the project documents are properly archived for future reference.

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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:
Steve Binion, PhD, BD
Janet Johnson, Abbott
Kerwin Kaufman, Roche
Valynda Machen, NAMSA
Peter Shearstone, Sysmex
Susan Tibedo, Abbott
Sandra White, ICON plc

Program Manager:
Carolyn Hiller, MDIC

FDA:
Zivana Tezak, PhD CDRH/OIR

Expert Advisors:
Susan Alpert, MD, PhD
Fred Lasky, PhD

What is the timeline for the deliverables of this project?

Deliverable		Preliminary Timing	Responsible
1	Data Gathering	Q1 2017	
2	Glossary of Terms	Q1 2017	
3	Defined change tool with simple rating system	Q2 2017	
4	Analysis of change tool and addition of adequate examples for each level in the tool	Q2 2017	
5	Examples of appropriate tests/studies or documentation for each change risk level example	Q2 2017	
6	Final Release of Tool	Q3 2017	
7	Conclusion of project	Q3 2017	