



MaRS | ENTREPRENEUR
WORKBOOKS

Emerging Life Sciences Series

Defining Your Target Product Profile: *In Vitro* Diagnostic Products

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Introduction

What is a target product profile?

A target product profile (TPP) is a key strategic document that provides a summary of the following:

- the product under development
- the product's desired characteristics and features
- the studies and activities that must be completed to demonstrate the product's performance, efficacy and safety
- the features of the product that provide a competitive advantage

A well-designed TPP provides a structure to ensure that the company embarks on a product development program that is efficient and yet defines a listing of all relevant medical, technical and scientific information required to reach the desired commercial development outcome. Historically, the US Food and Drug Administration (FDA) developed the concept of TPP to facilitate a communication strategy regarding a particular drug development program. However, many of the objectives provide sound guiding principles for development of diagnostic products or medical devices.

Benefits of a TPP

If used properly, a TPP can help address issues early in the product development process and prevent late-stage development failures. A TPP also provides various parties and stakeholders (e.g., management, board members, employees, advisors, investors, regulatory authorities, strategic partners) a clear statement of the desired outcome of the product development program. This can be used later to help assess elements of the process and track progress. The TPP is a dynamic strategic document that should be revisited during the course of development. Much of the information discussed in the TPP should be incorporated into your [business plan](#).

A TPP serves as a:

- strategic planning tool
- communication tool for discussions with regulatory authorities
- communication tool for discussions with investors, partners, employees and other stakeholders
- tool for communicating, supporting and tracking changes during the lifecycle of the development program

The FDA TPP document was specifically developed for therapeutic products to provide a format for discussions between a sponsor and the FDA. Based on this framework, this workbook has been developed to specifically assist companies embarking on the development of new *in vitro* diagnostic (IVD) products.

IVD products include reagents, instruments and systems intended to screen, diagnose or monitor a disease or condition. This workbook will help you put together a target product profile for *in vitro* diagnostic products (TPP-IVD).

There are three potential avenues to access the US market with a diagnostic depending on whether the product is an analyte specific reagent (ASR), a laboratory-developed test (LDT) or an IVD. Elements of the target product profile workbook and template are applicable to all three classes of diagnostics.



For a summary of the pertinent regulations of each of these three classes of diagnostics, read the document entitled "[Pathway to Commercialization for an in vitro Diagnostic \(IVD\) in the US.](#)"

Five key features of an IVD have been selected for developing the TPP-IVD:

1. Intended use statement
2. Summary and explanation of how the test works
3. Summary of the test procedure
4. Interpretation of results
5. Performance characteristics

These five sections were selected based on their importance when developing a [business plan](#). All sections provide an opportunity (see the accompanying workbook template) to describe the key [differentiating features](#) and competitive [positioning](#) of your product. The focus on competitive positioning will assist your company in communicating the value proposition, as you embark on [raising capital](#) and preparing for strategic discussions with [partners](#).

How to use these workbooks

1. Make it a team exercise—but make it quick!

We believe that much of the information you need is already known to your management team and advisors, so we recommend that you make the creation of your TPP-IVD a team effort. Remember, time is of the essence for high-tech start-ups and we encourage you to complete the workbook template thoroughly, but as efficiently as possible. The first version of your TTP-IVD should be no longer than eight to 12 pages. Use bullets and lists to accelerate the drafting of the first version.

2. Record and test your assumptions

As you go through the exercises, record and highlight key assumptions. Identify assumptions that will be tested (and validated or invalidated) through further market

research, as well as assumptions that will be tested through laboratory or clinical studies.

3. Use the icons for help

The MaRS workbooks are structured under the assumption that this is the first time you, the reader, has undertaken an exercise in of this nature. To help provide context for some of the ideas in these workbooks, we have clarified the ideas by defining key terms and offering real-world examples. In addition, we have provided links to articles provided by MaRS through the [Entrepreneur's Toolkit](#). For this reason, you may find it easiest to use these workbooks on a computer with an Internet connection.

Look for these icons:



denotes a key industry term that will recur in these workbooks



indicates an example drawn from a real-world business in order to illustrate an important idea



denotes a link to a more in-depth online article



appears wherever you are asked to record something while completing the exercises

Before you start

The following five steps will help you gather the data needed in order to commence these workbook exercises.

Note that the following approach applies to new IVD products where competitor products exist. Creating a TPP-IVD for a new clinical diagnostic (e.g., an emerging biomarker) remains a worthwhile exercise as it will help you organize your thoughts, outline the studies you will have to undertake and define milestones related to fundraising.

1. Broadly list all the potential usages of your proposed IVD product. Rank the potential usages and select an initial intended use. The selection of the initial intended use is one of the most critical strategic decisions for an early-stage



development company. Criteria to consider for selection of the initial intended use include:

- a. Will the intended use validate the product's clinical benefit(s)?
- b. Will the intended use clearly demonstrate a competitive advantage?
- c. Does the intended use provide an efficient path to regulatory approval?
- d. Does it lay the foundation for leveraging expanded IVD usages in the future?
- e. Does the intended use target a real market opportunity with revenues that will support the company's future growth?

While you may not be able to answer all of these questions at first, the exercise of defining a TPP-IVD provides a structured platform to test the initial intended use against key metrics.

2. Once you have selected an initial intended use, identify the competitive products that target the same market application. You can contact your MaRS advisor for assistance.
3. Research competitive IVD products based on intended use, technology, intended patient population, and where the test would be performed. Detailed information on competitive IVD products can be found in a variety of documents including the "Directions for Use" package inserts that are included with the diagnostic kit. These package inserts can be found through product websites or by accessing the approval and 510(k) clearance summaries posted on the FDA website at <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/default.htm>
4. Review and familiarize yourself with the contents on package inserts for competitive products. Highlight the areas where these competitive products have limitations and your product is designed to offer improved benefits.
5. Determine the laboratory and clinical studies needed to demonstrate your competitive differentiation. Even if you don't yet have a complete non-clinical and clinical testing plan, we recommend you outline how many studies you will need, the anticipated outcome from those studies and a prospective development timeline.

WORKBOOK:

Defining Your Target Product Profile: *In Vitro* Diagnostic Products

1. Intended use statement

In completing this section of the TPP-IVD, you will create a concise summary of the product under development. Note, this section is not about technology platforms or broad descriptions of opportunities across a range of indications and diseases.

In response to the following questions, provide a brief, focused description of your proposed final product.

- Is the test for screening, monitoring or diagnosis?
- What type (i.e., general category) of test is it?
- Is the test quantitative or qualitative?
- What is the specific analyte or risk factor of interest?
- What specimen is required for testing?
- What is the target population?
- How will the results of the test be used?



In the corresponding section of the workbook template, write one or two brief sentences in response to the questions above.

Review the example (on the following page) of Dako's HER2 FISH pharmDx™ Kit with regard to the intended use statement and indication for use.

**Example: Intended use statement and indication for use—HER2 FISH pharmDx™ Kit**

Dako has developed a molecular diagnostic kit for the detection of HER2 gene amplification in various cancers. The intended use statement in the package insert¹ reads:

"HER2 FISH pharmDx™ Kit is a direct fluorescence in situ hybridization (FISH) assay designed to quantitatively determine HER2 gene amplification in formalin-fixed, paraffin-embedded (FFRE) breast cancer tissue specimens and FFPE specimens from patients with adenocarcinoma of the stomach including gastro-esophageal junction.

HER2 FISH pharmDx™ Kit is indicated in adjunction to HercepTest™ in the assessment of patients for whom Herceptin™ (trastuzumab) treatment is being considered (see Herceptin™ package insert²)."

Sources:

¹<http://www.dako.com/ca/download.pdf?objectid=120858002>

²<http://www.gene.com/gene/products/information/pdf/herceptin-prescribing.pdf>

Note how the first sentence in the intended use statement answers the first six questions indicated above. The second sentence describes how the test results will inform physicians and patients. The HER2 FISH pharmDx™ test, along with the second diagnostic, HercepTest™, reflects the emerging trend in companion diagnostics to guide selection of patients for treatment with targeted drugs such as Herceptin™. The indication for use also directs the user to the package insert for the drug Herceptin™.

Consider the following points (if applicable) with regard to your own product:

- How well characterized and validated is the target analyte in terms of guiding the screening, monitoring or diagnosis of the disease?
- Is there an existing diagnostic kit that may serve as a predicate device for your regulatory strategy?
- Will additional diagnostic tests be required as adjuncts to your test before physicians gain a complete clinical picture? If yes, where will your test fit into the diagnostic testing protocols?
- How will the results of your diagnostic kit support clinical decisions to start, stop or change treatment of the patient?



Review the example of Cepheid's Xpert® MRSA/SA SSTI assay with regard to intended use statements.



Example: Intended use statement—Xpert® MRSA/SA SSTI assay

The diagnostics company Cepheid has developed a panel of molecular diagnostic tests for infectious diseases. The intended use for the Xpert MRSA/SA SSTI test includes the following description:

"The Cepheid Xpert MRSA/SA Skin and Soft Tissues Infection Assay (Xpert MRSA/SA SSTI Assay) performed in the GeneXpert® Dx System is a qualitative in vitro diagnostic test intended for the detection of Staphylococcus aureus (SA) and methicillin-resistant Staphylococcus aureus (MRSA) from skin and soft tissue infection swabs. The test utilizes automated real-time polymerase chain reaction (PCR) to detect MRSA/SA DNA. The Xpert MRSA/SA SSTI Assay is indicated for use in conjunction with other laboratory tests such as microbiology culture, and clinical data available to the clinician as an aid in the detection of MRSA/SA from skin and soft tissue infections. The Xpert MRSA/SA SSTI Assay is not intended to monitor treatment for MRSA/SA infections. Concomitant cultures for SA and MRSA are necessary to recover organisms for susceptibility testing or epidemiological typing."

Source: http://www.accessdata.fda.gov/cdrh_docs/pdf8/K080837.pdf

In this case, the intended use statement also clearly defines the instrument required to perform the test, the major contraindications, and complementary tests that may be required to fully inform the physician.

Consider the following points (if applicable) with regard to your own product:

- What are the contraindications for the test?
- Will the test work only with specific instrumentation? If yes, what instruments and devices are required?
- Are there specific patient characteristics that would identify patients most likely to be prescribed this test?

2. Summary and explanation of the test

In completing this section of the TPP-IVD, you will create a concise summary and explanation of the test and how the test results will be used. In response to the following questions, keep your answers brief:

- What is the test intended to detect and what is the scientific basis for the detection?
- Will a specific device or software be required to complete the test?
- When would the test be used?
- What will the test accomplish?
- When should the test not be used?



In the corresponding section of the workbook template, write one or two brief sentences in response to the questions above.

Review the example (on the following page) of the BinaxNOW[®] Malaria Test with regard to the summary and explanation of the test. Note how the above questions were addressed in its package insert.



Example: Summary and explanation of the test— BinaxNOW® Malaria test

Inverness Medical sells the BinaxNOW Malaria test kit. This was the first FDA-approved product cleared for the detection and identification of parasites that cause malaria. A full description of the test summary and principles can be found in the BinaxNOW [package insert](#):

"The BinaxNOW® Malaria Test is a simple, rapid test for the diagnosis of malaria using whole blood collected by finger stick or venous draw. The dual line format allows for detection of malaria parasites and for differentiation of Plasmodium falciparum (P.f.) from other less virulent malaria species. The test cannot distinguish a single species malaria infection from a mixed species infection. Good clinical practice warrants that microscopy be performed to make this determination, as well as to differentiate among the non-falciparum Plasmodium species."

"The BinaxNOW® Malaria Test is an immunochromatographic membrane assay that uses monoclonal antibodies to detect Plasmodium falciparum antigen and pan-malarial antigen (an antigen shared by all Plasmodium species causing human malaria) in venous and capillary whole blood specimens. These antibodies, and a control antibody, are immobilized on a membrane support as three distinct lines and are combined with a sample pad, which is impregnated with visualizing particles conjugated to control and anti-malaria antibodies, to create a test strip. This test strip is mounted in a book-shaped, hinged test device, along with wash and absorbent pads, intended to aid in the clearing of the membrane when the device is closed."

This test represented an important new tool for diagnosing malaria in parts of the world that did not have qualified personnel to read microscopic smears. The statements in the summary clearly indicate the intended target and, in addition, highlight some of the limitations of the assays.

Source:

<http://www.alere.com/us/en/product-details/binaxnow-malaria.html>

Consider the following points (if applicable) with regard to your own product:

- Will this be a laboratory test, point-of-care test or one for use at home?
- What level of expertise will be required to perform the test correctly?
- What controls have been or will need to be included in the test kit?
- What are the potential limitations of the test?



- If the tests results are negative, what does that mean for the patient and their physician?

Review the example of Abbott's RealTime HBV assay with regard to the summary and explanation of the test.



Example: Summary and explanation of the test— RealTime HBV assay

The intended use for Abbott's RealTime HBV assay is as an aid to the management of patients with chronic hepatitis B virus (HBV) infection who are undergoing antiviral therapy.

The following is an extract from the package insert and exemplifies some key considerations for this assay. (See the full [package insert](#) for the complete version of the summary and explanation of use section.)

To address when the test would be used and what the test results would accomplish, the package insert states:

"Quantitation of HBV DNA is important in the evaluation and management of patients with chronic HBV infection. Current guidelines recommend HBV viral load to determine which chronic HBV patients should be treated and to monitor their response to therapy. A low baseline viral load has been shown to be predictive of response to therapy. Conversely, a high baseline viral load is predictive of resistance to therapy as well as a relapse following therapy, and has also been found to be an independent risk factor for hepatocellular carcinoma. Current treatment options include interferon, peginterferon and antiviral drugs such as lamivudine, adefovir and tenofovir."

The value of the test results and the impact of low and high results are clearly described.

In another section of the summary, the package insert explains that the assay was standardized against the World Health Organization (WHO) International Standard for hepatitis B virus DNA.

Source:

http://www.abbottmolecular.com/static/cms_workspace/package_inserts/HBV%20US%20package%20insert%2009_22_10.pdf

Consider the following points (if applicable) with regard to your own product:

- Will this test be used to guide the treatment of patients with specific drugs?
- Are there guidelines from organizations such as WHO that will be used to standardize and validate your test?
- Does your summary communicate the value of the test to the clinician?

3. Summary of test procedure

The simplicity or complexity of the test procedure will determine whether your test is appropriate for your target location for testing.

For tests that are intended to be used by patients (e.g., glucose monitoring test strips), simplicity of use will be a key feature for robustness and reliability.

Complex diagnostic tests which require multiple steps and numerous controls (e.g., molecular diagnostic tests) are intended for use in clinical laboratories, under the supervision of qualified laboratory personnel.

In completing this section of the TPP-IVD, you will create a concise summary of the test procedure. In response to the following questions, keep your answers brief:

- What samples, reagents, equipment and controls are required to perform the test?
- What are the main steps in the procedure, from sample collection to final results?
- What is the target turnaround time from sample collection to the final results?
- Are there any special precautions that need to be considered?



In the corresponding section of the workbook template, write a brief list of points in response to the questions above. Highlight areas of proposed competitive strength.

Review the example (on the following page) of LifeScan's OneTouch® UltraMini® Meter with regard to the summary of test procedure. This product is illustrative of test kits intended for use at home.

**Example: Summary of test procedure—OneTouch® UltraMini® Meter**

LifeScan's OneTouch UltraMini Meter is intended to be used by patients at home for the ongoing monitoring of blood glucose in the management of diabetes. Although the test is designed to be as simple as possible, the owner's manual lists seven different components that are required to complete the test. The following is an excerpt from the manual:

"To test with the OneTouch UltraMini System, you will need the following:

- a) OneTouch UltraMini Meter (battery included)*
- b) OneTouch® Ultra® Control Solution*
- c) OneTouch® Lancing Device. If another type of lancing device was included, see the separate instructions that came with that lancing device.*
- d) OneTouch® AST™ Clear Cap*
- e) OneTouch® UltraSoft® Sterile Lancets*
- f) Carrying Case*
- g) You will also need OneTouch® Ultra® Test Strips. Some kits do not include strips. Strips are sold separately."*

See the [owner's manual](#) to review the use of illustrations to guide the patient through the various steps of properly collecting a blood sample, using the instrument and interpreting the data.

Note the consistent branding of the various components, including the disposable components that represent recurring revenue streams.

Source: <http://www.onetouch.com/onetouch-ultraminif>

Consider the following points (if applicable) with regard to your own product:

- How many separate components will be developed and sold?
- Have you developed a branding strategy for your product and its components?
- Will there be reagents or equipment that will be purchased from other vendors and how will your product integrate?
- How will you ensure the continuity of supply and support for reagents or supplies you do not provide?

If your company is developing a more complex molecular diagnostic test, review the example (on the following page) of Abbott's RealTime HBV assay with regard to the summary of test procedure.



**Example: Summary of test procedure—RealTime HBV assay**

The intended use for Abbott's RealTime HBV assay is as an aid to the management of patients with chronic hepatitis B virus (HBV) infection who are undergoing antiviral therapy. See the full [package insert](#) for the complete version of the test procedure.

In the package insert, the information related to the test procedure lists seven different types of reagents. These include internal controls, amplification reagent packs, negative controls, low positive controls, high positive controls and two calibrator kits.

In the summary for the test procedure, various sections describe special precautions such as protection for technicians handling potentially infectious components, and how to avoid cross contamination.

The complexity of the test demands a high skill level to properly execute the assay and qualified laboratory facilities to perform the test.

Source:

http://www.abbottmolecular.com/static/cms_workspace/package_inserts/HBV%20US%20package%20insert%2009_22_10.pdf

Consider the following points (if applicable) with regard to your own product:

- Is the complexity or simplicity of the test appropriate for the intended location for executing the test?
- What auxiliary reagents and standards are needed for quality-assurance testing and calibration?
- If your competitors require reagents that are temperature-sensitive and need to be frozen or refrigerated to be stored and transported, can you offer a competitive advantage by eliminating the need for this expensive step?

4. Interpretation of results

The results from a clinical diagnostic test may require visual observations or manual calculations, or they may be analyzed automatically by a computer. Regardless of how the results are reported, this section of the TPP-IVD should include a brief description of key steps in the calculations.

In completing this section of the TPP-IVD, you will provide guidance on how the test results will be generated and how to interpret them. At a minimum, this section should answer the following questions:

- How are the results calculated?
- What constitutes a positive or negative test result?
- When is a test result considered abnormal and clinically significant?
- When is a test result considered invalid?
- What are the general limitations of the test?



In the corresponding section of the workbook template, write a brief list of points in response to the questions above.

Consider the following points (if applicable) with regard to your own product:

- What other factors (e.g., the patient's medical history) need to be considered when interpreting the results?
- What quality control measures need to be included to support the interpretation of the results?
- If there are ranges of values, how were these ranges established?

The interpretation of results assumes the results are valid. However, it is not uncommon for external factors to influence the outcome of test. These factors generally fall under the category of limitations. Review your competitors' products to identify common limitations as well as areas of potential competitive advantage for your IVD product.

The following is a checklist of potential limitations that might impact test results. It is provided as guideline and is not exhaustive.

- ☐ Multi-step process that requires highly specialized training
- ☐ Incorrect sample collection
- ☐ Improper sample handling
- ☐ Interference encountered by the presence of drugs, antibodies or other agents
- ☐ Temperature sensitivity of the assay or reagents
- ☐ Dependence on the performance of specific instrumentation
- ☐ Lack of data to support testing of certain patient populations



5. Performance characteristics

In completing this section of the TPP-IVD, you will summarize the target performance specifications that your product needs to meet in order to gain approval and win a competitive advantage. This will help you build a roadmap of the studies required to generate the data to support and validate your specifications.

Review this checklist of the typical performance characteristics for a diagnostic test:

- ☐ Sensitivity
- ☐ Specificity
- ☐ Predictive values
- ☐ Reproducibility
- ☐ Repeatability
- ☐ Stability
- ☐ Interference
- ☐ Limits of the detection and measurement range
- ☐ Earliest clinical detection in comparison to reference tests
- ☐ 95% confidence interval

In addressing the following questions, keep your answers brief and focused:

- What are the target specifications for key performance characteristics?
- What studies will be required to test the performance?



In the corresponding section of the workbook template, write a brief list of points in response to the questions above.

Consider the following points (if applicable) with regard to your own product:

- What performance features differentiate your product from the competition?
- What reference standards will be used as comparisons?
- Is there a predicate device against which the performance standards will be compared?