Welcome Guide

Prosigna® is indicated for use in postmenopausal women with HR-positive, node-negative or node-positive (1–3 positive nodes) early stage (stages I and II) breast cancer to be treated with adjuvant endocrinotherapy. The Prosigna Assay is 510(k)-cleared for in vitro diagnostic use, in conjunction with the nCounter® Dx Analysis System. See Package Insert at www.Prosigna.com for details.

Table of Contents

Prosigna Overview ..........................2
Planning Your Lab Space .................4
  • Example Lab Layouts .................5
  • Guidance on Lab Materials ..........5
Ancillary Equipment ........................6
  • Common Questions When
    Selecting Ancillary Equipment ........6
  • Ancillary Equipment ...................7
Preparing for Installation and Training ....7
  • Pre-Installation .......................7
  • Pre-Training .........................7
  • Training Kit Storage Conditions ......8
Training Logistics and Schedules ........9
  • Example Training Schedules ........9
Validation Overview .....................12
How to Contact Technical Support ........13
Prosigna Patient Support Program (PPSP) ....14
  • Common Questions When
    Participating in PPSP ...............14
Establishing Reimbursement Logistics ......15
  • Overview of NPI and Taxonomy Codes 15
How to Create a New Organizational NPI ....17
  • Adding an Additional Taxonomy
    to Your NPI .........................27
  • Overview of MolDx and
    the Z-Code Identifier ..............28
  • How to Register with McKesson
    Diagnostic Exchange ..............30
  • Adding the Prosigna Test to
    McKesson Diagnostic Exchange ....37
Prosigna Overview
The purpose of this document is to assist you in establishing the Prosigna® Breast Cancer Prognostic Gene Signature Assay in your lab. Before you can begin running the Prosigna Assay, you will need to prepare your lab space and ensure that you have all of the required ancillary equipment on-hand. Once you are ready, NanoString will install your nCounter® Dx Analysis System and provide on-site training. You may be required to perform a verification and validation study once your training is complete and before you begin running the Prosigna assay on patient samples based on regulations applicable to your laboratory (CLIA and others as applicable). Each section in this guide offers helpful information and guidance through each phase of the Prosigna set-up process (FIGURE 1).

The Prosigna Breast Cancer Prognostic Gene Signature Assay is an *in vitro* diagnostic assay performed on the NanoString nCounter Dx Analysis System using RNA isolated from FFPE breast tumor tissue previously diagnosed as invasive breast carcinoma. This qualitative assay utilizes gene expression data weighted together with clinical variables to generate a risk category and numerical score that assesses a patient’s risk of distant recurrence of disease.

Before the test can be performed, a pathologist examines a hematoxylin and eosin (H&E) stained slide to identify and measure the area of invasive breast carcinoma suitable for the test. A trained technologist then macrodissects the tumor tissue on the unstained slides, essentially collecting the tumor tissue and removing the non-tumor tissue from each section. The tumor tissue is then digested overnight, and the RNA is isolated using a column-based RNA extraction kit. The isolated RNA is hybridized with NanoString probes overnight and tested on the nCounter

### Prosigna Enablement

![Prosigna Enablement Diagram](image)

**FIGURE 1:** Setting up your lab for Prosigna involves several phases: instrument purchase, site preparation, system installation, and training. You may also be required to perform a validation of the assay before running patient samples based on regulations applicable to your laboratory (CLIA and others as applicable).
Dx Analysis System to provide the test results, including the Prosigna Score and risk category (FIGURE 2).

Please note that a pathologist is not required to perform the technical components of the Prosigna assay outlined in FIGURE 2. Depending on local regulations, a staff pathologist may be required in order for your lab to receive a patient’s tissue sample; however, the assay itself may be performed by professional laboratory personnel who are trained in standard molecular biology techniques in high complexity CLIA labs. Please see Training Logistics and Schedules (Page 9) for more information on Prosigna training, or contact NanoString for further assistance.

**Prosigna Workflow**

**Day 1**
- **Macrodissection**
  - Hands on: 1 hour

**Day 2**
- **RNA Isolation**
  - Hands on: 2 hours
- **Setup Hybridization**
  - Hands on: 30 minutes
- **Hybridization**
  - 65°C Incubation
  - Overnight, 15-21 hours
  - Optional: Store RNA at -70°C or below

**Day 3**
- **Load Samples and Run Prep Station**
  - Hands on: 30 min
  - Run time: 1.5-2.5 hours
- **Run Digital Analyzer**
  - Hands on: 10 min
  - Run time: 1-4.5 hours

**Reports are ready!**

**FIGURE 2:** The Prosigna workflow is divided into 3 days. On the first day, tumor tissue is macrodissected and an overnight enzymatic tissue digestion is prepared. On the second day, RNA is isolated from the digested tumor tissue, and samples are then hybridized with NanoString probe complexes overnight. On the last day, samples are loaded onto the NanoString nCounter Dx Analysis System for quantification, and the Prosigna reports are generated.
Planning Your Lab Space

If you are creating a new lab space for Prosigna, this section provides guidance on your lab layout and lab surface materials.

**FIGURE 3:** Example lab layout for Prosigna. Cold storage for 4°C and -20°C can be installed under a lab bench if desired. Uninterrupted Power Supply (UPS) is not required but strongly recommended for your nCounter system.
Example Lab Layouts
There are many options for configuring your lab space for Prosigna. The minimal requirements for a lab space are as follows:

- A main workspace for performing macrodissection, RNA isolation, and hybridization (FIGURE 3). You may choose to designate one area for all three tasks or separate areas for each.
- Bench space for the nCounter Dx Analysis System. The recommended site dimensions for the Prep Station are 47 in. x 30 in. x 46 in. For the Digital Analyzer, the recommended dimensions are 30 in. x 25 in. x 35 in.
- Bench space for the ancillary equipment required to perform the Prosigna assay (e.g. benchtop centrifuges, heat blocks, vortexer, etc.).
- Storage space for Prosigna kits and consumables. Different components of the assay will require storage at either room temperature, 4°C, -20°C, and -80°C.
- Storage space for ancillary materials and consumables. You will likely want to stock your lab with a supply of consumables such as pipette tips, microfuge tubes, gloves, etc.
- Flammables storage. The Prosigna assay requires the use of 100% ethanol. Please consult with your institution’s biosafety guidelines to ensure proper storage and handling.

Guidance on Lab Materials
Lab benches:

- Bench top surface should be non-absorbent and chemically-resistant. Phenolic resin is a common choice for many labs.
- Lab benches should be capable of supporting 300 lb. (136 kg) for the Prep Station and 150 lb. (68 kg) for the Digital Analyzer.
- The Digital Analyzer should be well-isolated from large sources of vibration such as HVAC ducts or centrifuges.

Lab Flooring:

- Flooring material should be non-absorbent and chemically-resistant.
- Laboratory-grade flooring is not required for the Prosigna Assay.
- Many labs choose tile flooring for ease of cleaning and durability.

Power Source:

- Surge-protected, 610W.
- An Uninterruptable Power Supply (UPS) is strongly recommended.
Ancillary Equipment

Running the Prosigna Assay requires some basic lab equipment in order to prepare and process your samples. The list on the following page contains recommendations for the ancillary equipment and reagents necessary to perform the Prosigna assay, however equivalent products may be substituted at your convenience. If you have questions about alternatives, we will be happy to review product specifications with you to help select the appropriate equipment for your lab.

Common Questions When Selecting Ancillary Equipment

Do I need to buy a computer to use with the nCounter Dx Analysis System?

Users will need to provide their own computer system to use with the nCounter Dx Analysis System, however the computer does not need to be dedicated exclusively to the nCounter instrument. If you have a local network set up in your lab, you can network the nCounter Dx Analysis System and then use any networked computer to access and print your Prosigna reports.

What kind of computer should I use to generate and print my Prosigna reports?

Either a Mac or a PC is compatible with our instruments. The only system requirement is that the computer must have one of the following Web Browsers installed: Internet Explorer 10.0 or 9.0, Firefox 21.0 or 20.0, Chrome 27.0 or 26.0, or Safari 7.0 or 5.1. Internet access is not required.

Do I need to buy a thermal cycler for overnight hybridizations?

A thermal cycler is not required for the Prosigna assay. A heat block with a heated lid is often a more cost effective option and can be used for overnight hybridizations as long as it meets the required specifications for Prosigna. Note that while the cost for a thermocycler will be higher, it will allow for up to 96 samples (or 8 cartridges of 12 samples each) to be hybridized in parallel overnight. In contrast, most heat blocks can reasonably accommodate 30 samples (2.5 cartridges of 12 samples each) to be hybridized in parallel.

Additionally, strip tubes must be cut in half when using a heat block to accommodate the smaller heat block.

Can I purchase ancillary equipment that is different from what is listed on your equipment list?

Yes. We can provide an easy recommended shopping list for labs who wish to purchase all ancillary items at once. If you have other preferred vendors or existing lab equipment, you are welcome to use alternative products as long as they will meet the specifications for Prosigna.

<table>
<thead>
<tr>
<th>Capital Equipment</th>
<th>Individual Costs</th>
<th>Total Price Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Centrifuge with Rotor for 30 x 2 mL tubes</td>
<td>$4,600–$5,600</td>
<td></td>
</tr>
<tr>
<td>Additional Rotor for Microplates</td>
<td>$1800–$2,200</td>
<td></td>
</tr>
<tr>
<td>Spectrophotometer</td>
<td>$4,500–$5,500</td>
<td></td>
</tr>
<tr>
<td>Laboratory Freezer (-80°C)</td>
<td>$13,500–$16,500</td>
<td></td>
</tr>
<tr>
<td>Laboratory Freezer (-24 to -15°C)</td>
<td>$1,300–$1,500</td>
<td></td>
</tr>
<tr>
<td>Laboratory Refrigerator (0-10°C)</td>
<td>$1,500–$1,800</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other Ancillary Equipment</th>
<th></th>
<th>$2,800–$3,500</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consumables (pipette tips, microfuge tubes, etc.)</td>
<td>$1,150–$1,400</td>
<td></td>
</tr>
<tr>
<td>Reagents/Supplies (chemicals, storage racks, glassware)</td>
<td>$620–$750</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>$31,770–$38,750</td>
</tr>
</tbody>
</table>

FIGURE 4: Approximate costs for each category of items needed
Preparing for Installation and Training

Your trainer will reach out to you before your instrument is installed to begin a conversation about your installation and training schedule. Your trainer will also send you the Dx Enablement Checklist. This checklist includes all of the environmental, network, ancillary equipment, and reagent requirements needed to perform your Diagnostic Installation and Training.

Upon confirmation that all required equipment for installation is on-site and ready for use, your 3-day installation will be scheduled. A NanoString Field Service Engineer will then arrive on the scheduled date to perform the Operational Qualification (OQ) and Performance Qualification (PQ) of your nCounter instruments. These qualifications will ensure that both the hardware and software on your instrument are working appropriately. Once the installation is completed, your nCounter Dx Analysis System is ready for the training.

If you have any questions about the installation procedure, please contact your NanoString trainer at DxSupport@NanoString.com.

Ancillary Equipment

All ancillary equipment must be available in the lab before your training can be scheduled. If you need help, NanoString can provide guidance as you select the required ancillary equipment for Prosigna. Our trainers are happy to answer any questions about lab set-up, equipment, scheduling, and training. For your convenience, the approximate costs for each category of items that you will need is listed (FIGURE 4). If you have questions about selecting equipment or other items for use with Prosigna, please contact your NanoString trainer.

How can I check if my lab equipment meets the specifications for use with Prosigna?

Consult the Dx Enablement Checklist provided by your NanoString trainer for all equipment requirements, or consult directly with your trainer. You may also email questions to DxSupport@NanoString.com.

Pre-Training

Upon confirmation that all required equipment and reagents for training are on-site and ready for use, your training can be scheduled. Inform your trainer of any important schedule restrictions for any of the training participants, and we will be happy to customize a training schedule for your site. NanoString can accommodate up to 3 people participating in the hands-on portions of the Prosigna training, however, anyone is welcome to observe and ask questions.

Once you have scheduled your training, NanoString will send you Prosigna Training Kits and a Roche FFPET RNA isolation kit for use during the training (see below for storage conditions of the training kit components). Additionally, NanoString provides sample slides to use for the training. The slides are located in the Prep Pack in a blue slide case under the flap that states ‘lift for additional contents’ in the center of the box. For each set of slides, there will be one H&E stained slide and one or more unstained slides.
Training Kit Storage Conditions

Once you receive the training shipment from NanoString, it is important that all training materials are stored properly upon receipt. Please consult the table below for proper storage and handling descriptions for each component.

<table>
<thead>
<tr>
<th>Item</th>
<th>Storage Temperature</th>
<th>Description</th>
<th>Dimensions</th>
</tr>
</thead>
<tbody>
<tr>
<td>CodeSet</td>
<td>-80 °C or below</td>
<td>Capture Probes, Reporter Probes, and Reference Sample</td>
<td>Length: 5.1 in.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Width: 2.5 in.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Height: 1.9 in.</td>
</tr>
<tr>
<td>Prep Plates</td>
<td>2-8 °C</td>
<td>96-well plates with all reagents. Plates must be stored upright for optimal performance</td>
<td>Length: 5.1 in.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Width: 3.4 in.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Height: 0.75 in.</td>
</tr>
<tr>
<td>Cartridges</td>
<td>-20 °C or below</td>
<td>Cartridges in individual foil-sealed pouches</td>
<td>Length: 6.0 in.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Width: 3.75 in.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Height: 0.44 in.</td>
</tr>
<tr>
<td>Prep Pack</td>
<td>Room temperature (15-25 °C)</td>
<td>Includes keyed strip tubes, hybridization buffer, tips and tip sheathes, etc.</td>
<td>Length: 7.0 in.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Width: 5.4 in.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Height: 3.5 in.</td>
</tr>
<tr>
<td>Roche FFPET RNA Isolation Kit</td>
<td>Room temperature (15-25 °C)</td>
<td>Includes all buffers required for RNA isolation</td>
<td>Length: 7.0 in.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Width: 7.0 in.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Height: 4.5 in.</td>
</tr>
</tbody>
</table>
Training Logistics and Schedules

NanoString is committed to offering a variety of on-site training options to fit your needs. Our team of scientists and trainers will provide you with the knowledge and skills that you need to advance your diagnostic capabilities.

Prosigna training is intended for professional laboratory personnel who are trained in standard molecular biology techniques in high complexity CLIA labs. After your instrument has been installed by a NanoString Field Service Engineer, a certified NanoString trainer will travel on-site to train up to 3 users. Each training begins with a brief overview presentation, followed by a hands-on demonstration of the Prosigna assay. Your trainer will guide users through each step of the Prosigna assay, and each training participant will conduct his or her own Prosigna test from start to finish. At the end of the training, each trainee will generate his or her own Prosigna report and receive a Record of Completion.

The duration of the training will depend on the number of trainees present. Typically, NanoString trains up to 3 users over a period of 3–4 days (see Example Training Schedules beginning on the following page). It is imperative that all trainees are present for all portions of the training, so please communicate any schedule restrictions with your trainer in advance of the training, and we will be happy to accommodate your needs.

Example Training Schedules

A typical training schedule for 1 Trainee.

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
</tr>
</thead>
</table>
| **1:00 PM–2:00 PM**  
Introductions & PowerPoint Presentation   | **8:00 AM–8:30 AM**  
Demo hybridization to Prep Station         | **8:00 AM–8:30 AM**  
Trainee 1: Hybridization to Prep Station   |
| **2:00 PM–3:30 PM**  
Macrodissection  
(12-23 hour digest)                        | **8:30 AM–10:30 AM**  
RNA Isolation                              | **8:30 AM–9:30 AM**  
Dx Administrators  
Discuss Dx Administrator privileges and Prosigna verification/validation plan |
| **3:30 PM–4:00 PM**  
Demo hybridization setup  
(15-21 hour hybridization)                  | **11:00 AM–11:15 AM**  
Demo hybridization to Digital Analyzer      | **11:00 AM–11:15 AM**  
Trainee 1: Hybridization to Digital Analyzer |
| **4:00 PM–4:15 PM**  
Demo Prep Station, O-ring lubrication, and downloading log files | Break                                      | Break                                      |
| **3:00 PM–3:45 PM**  
Trainee 1: Set up hybridization  
(15-21 hour hybridization)                  | **3:00 PM–3:30 PM**  
Review reports  
Complete training documents                 | Any final questions?                       |

Day 1 Training Complete

Day 2 Training Complete

All Training Complete
A typical training schedule for 2 Trainees.

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1:00 PM–2:00 PM</strong></td>
<td><strong>8:00 AM–8:30 AM</strong></td>
<td><strong>8:00 AM–8:30 AM</strong></td>
<td><strong>8:30 AM–9:30 AM</strong></td>
</tr>
<tr>
<td>All Trainees: Introductions &amp;</td>
<td>All trainees</td>
<td>Trainee 1: Hybridization to</td>
<td>Print and review reports</td>
</tr>
<tr>
<td>PowerPoint Presentation</td>
<td>Demo hybridization to Prep</td>
<td>Prep Station</td>
<td>Complete training documents</td>
</tr>
<tr>
<td></td>
<td>Station</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>2:00 PM–4:00 PM</strong></td>
<td><strong>8:30 AM–10:30 AM</strong></td>
<td><strong>8:30 AM–9:30 AM</strong></td>
<td><strong>Any final questions?</strong></td>
</tr>
<tr>
<td>All Trainees: Macrodisssection</td>
<td>All trainees</td>
<td>Dx Administrators: Discuss Dx</td>
<td></td>
</tr>
<tr>
<td>(12-23 hour digest)</td>
<td>RNA Isolation</td>
<td>Administrator privileges and</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prosigna verification/validation plans</td>
<td></td>
</tr>
<tr>
<td><strong>4:00 PM–4:30 PM</strong></td>
<td><strong>11:00 AM–11:15 AM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Trainees: Demo hybridization setup (15-21 hour hybridization)</td>
<td>All Trainees: Demo hybridization to Digital Analyzer</td>
<td><strong>11:00 AM–11:15 PM</strong></td>
<td>Trainee 1: Hybridization to Digital Analyzer</td>
</tr>
<tr>
<td></td>
<td><strong>Break</strong></td>
<td><strong>11:00 AM–11:15 PM</strong></td>
<td></td>
</tr>
<tr>
<td><strong>4:30 PM–4:45 PM</strong></td>
<td><strong>3:00 PM–3:45 PM</strong></td>
<td><strong>11:15 AM–11:45 PM</strong></td>
<td></td>
</tr>
<tr>
<td>All Trainees: Demo Prep Station</td>
<td>Trainee 1: Set up hybridization</td>
<td>Trainee 2: Hybridization to</td>
<td></td>
</tr>
<tr>
<td>O-ring lubrication &amp; downloading log files</td>
<td>(15-21 hour hybridization)</td>
<td>Prep Station</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Break</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>3:45 PM–4:30 PM</strong></td>
<td><strong>2:30 PM–2:45 AM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trainee 2: Set up hybridization</td>
<td>Trainee 2: Hybridization to</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(15-21 hour hybridization)</td>
<td>Digital Analyzer</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Day 1 Training Complete</strong></td>
<td><strong>Day 2 Training Complete</strong></td>
<td><strong>Day 3 Training Complete</strong></td>
<td><strong>All Training Complete</strong></td>
</tr>
</tbody>
</table>
A typical training schedule for 3 Trainees.

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
</tr>
</thead>
</table>
| 1:00 PM–2:00 PM  
All Trainees:  
Introductions & PowerPoint Presentation | 8:00 AM–8:30 AM  
All Trainees:  
Demo hybridization to Prep Station | 8:00 AM–8:30 AM  
Trainee 1:  
Hybridization to Prep Station | 8:00 AM–8:30 AM  
Trainee 3:  
Hybridization to Prep Station |
| 2:00 PM–4:00 PM  
All Trainees:  
Macrodissection (12-23 hour digest) | 8:30 AM–10:30 AM  
All Trainees:  
RNA Isolation | Break | 8:30 AM–9:30 AM  
Dx Administrators:  
Discuss Dx Administrator privileges and Prosigna verification/validation plans |
| 4:00 PM–4:30 PM  
All Trainees:  
Demo hybridization setup (15-21 hour hybridization) | 11:00 AM–11:15 AM  
All Trainees:  
Demo hybridization to Digital Analyzer | 11:00 AM–11:45 AM  
Trainee 1:  
Hybridization to Digital Analyzer | Break |
| 4:30 PM–4:45 PM  
All Trainees:  
Demo Prep Station O-ring lubrication & downloading log files | Break | Trainee 2:  
Hybridization to Prep Station | 11:00 AM–11:15 AM  
Trainee 3:  
Hybridization to Digital Analyzer |
| 3:00 PM–3:45 PM  
Trainee 1:  
Set up hybridization (15-21 hour hybridization) | Break | Break | 3:30 PM  
All Trainees:  
Review reports for all trainees. Complete training documents for all trainees |
| 3:45 PM–4:30 PM  
Trainee 2:  
Set up hybridization (15-21 hour hybridization) | 2:45 PM–3:00 PM  
Trainee 2:  
Hybridization to Digital Analyzer | Break | Any final questions? |
| Day 1 Training Complete | Day 2 Training Complete | Day 3 Training Complete | All Training Complete |
Validation Overview

After the Prosigna training, you may verify the precision and accuracy of the Prosigna Assay as established in the product literature. Please follow your institution's requirements when planning your validation procedure. NanoString will provide up to 70 tests including synthetic RNA with known values for laboratory verification of performance characteristics, however you must provide the tissue samples that you will use during your validation process. If you are unable to use your own samples, you may coordinate with another site to exchange tissue, or you may purchase tissue from outside tissue vendors.

Purchasing tissue from outside suppliers is not required and the following commercial suppliers can provide tissue samples. NanoString does not recommend any one supplier above any others.

If you are ordering tissue samples to be used in your Prosigna verification/validation, it is recommended that the samples meet the indications for use with Prosigna, however the tissue selection for your verification/validation is ultimately up to you and your institution. The indications for use are listed in the Prosigna Package Insert (LBL-C0223), Page 1, Section 1 “Intended Use/Indications for Use”.

Additionally, when securing tissue to be used with the Prosigna assay there are clinical parameters that must be known for each sample to qualify for testing. Below are these clinical parameters as well as tissue requirements to keep in mind when acquiring tissue:

Prosigna sample specifications to keep in mind are:
- Gross Tumor Size must be known
- Nodal status must be known and \( \leq 3 \) positive nodes
- Unstained slides are 10 \( \mu \)m sections
- Tumor surface area must be \( \geq 4 \text{mm}^2 \)
- Percent tumor cellularity must be \( \geq 10\% \)

<table>
<thead>
<tr>
<th>Tissue Supplier</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>BioPartners</td>
<td><a href="http://biopartners.science/">http://biopartners.science/</a></td>
</tr>
<tr>
<td>Analytical Biological Services Inc.</td>
<td><a href="http://www.absbio.com/">http://www.absbio.com/</a></td>
</tr>
<tr>
<td>Bioreclamation IVT</td>
<td><a href="http://www.bioivt.com/">http://www.bioivt.com/</a></td>
</tr>
</tbody>
</table>
How to Contact Technical Support

If you have questions about the Prosigna assay or need assistance while running the test, our team of expert scientists will provide up-to-the-minute support for you and your lab. Contact Technical Support at DxSupport@NanoString.com or call us at 1-888-358-6266 for immediate assistance. Our Technical Service Scientists are standing by from 7 AM to 5 PM Pacific Standard Time to assist you.

If you need assistance with a run on either the Prep Station or the Digital Analyzer, please download the relevant instrument log files and email them along with your inquiry to DxSupport@NanoString.com.
Prosigna Patient Support Program (PPSP)
The Prosigna Patient Support Program (PPSP) is a comprehensive program designed to support you and your eligible patients, and your account manager will work with you to schedule a presentation overview of the PPSP. The PPSP Program Representatives will help you with each patient’s enrollment into the program and provide you detailed information on your patient’s coverage for Prosigna. The PPSP will also determine whether individual patients meet the program’s eligibility requirements for the patient assistance program (PAP) or Product Replacement Programs (PRP).

Common Questions When Participating in PPSP

What is the Prosigna Patient Support Program (PPSP)?
The PPSP has Program Representatives that are available to answer questions and the program offers a number of unique services including:
• Reimbursement assistance
• Insurance verifications
• Prior authorization and appeals process information/support
• Free product assistance – PAP (if eligible)
• Product replacement – PRP (if eligible)
• All services are provide free of charge

Who is eligible for your Free Product Program (PAP)?
If a patient is functionally uninsured or does not have coverage for Prosigna, and meets certain eligibility requirements, she may receive a free Prosigna test. Please note that the patient or her insurance plan cannot be billed for the free test.

Eligibility:
• No insurance coverage, or deemed functionally uninsured by the patient’s health plan
• US Resident
• Patient’s annual household income is ≤ 600% of the Federal Poverty Level
• If all eligibility criteria are met, a free test kit is sent to the selected lab for the patient’s samples

Why should I have a benefits verification completed for my patients?
A benefits verification will help you and the patient understand how Prosigna may be covered by the patient’s insurance plan. The PPSP Counselors can research your patient’s coverage to identify the requirements for covering Prosigna. In performing the benefits verification, if a prior authorization is required, our program representatives can assist with submitting a prior authorization to the payer per the payer’s mandated process. Further, our program representatives can also assist in the appeals process if that is necessary.
Establishing Reimbursement Logistics

Overview of NPI and Taxonomy Codes

What is an NPI?
The National Provider Identifier (NPI) was adopted and became effective May 23, 2007 as the standard unique health identifier for health care providers to carry out a requirement in the Health Insurance Portability and Accountability Act of 1996 (HIPAA) for the adoption of such a standard.

Who is required to have an NPI?
An entity who meets the definition of a “health care provider”—that is, any provider of medical or other health services, and any other person or organization that furnishes, bills, or is paid for health care in the normal course of business—is eligible to receive a provider ID, or NPI. Under HIPAA, a covered health care provider is any provider who transmits health information in electronic form in connection with a transaction for which standards have been adopted. These covered health care providers must obtain an NPI and use this number in all HIPAA transactions. The NPI may also be used on paper claims, but HIPAA does not govern that method of submitting claims.

Are there different types of NPIs?
There are two different types of NPIs, individual and organizational. These used to be referred to as Type 1 and 2. An organization may be one of several types:

• Multi-Specialty Group: Groups having members with more than one Taxonomy
• Single-Specialty Group: Groups having members with one Taxonomy
• Multiple Single Specialty: Groups having more than one location and the members have one Taxonomy

Does the NPI replace the Tax Identification Number (TIN)?
No. The NPI is not designed to replace the provider’s TIN, nor is the NPI designed to correspond to the TIN. The NPI and TIN must show the same Name, Entity status and address. If the two don’t match, claims will be rejected by the payer.

What is a taxonomy code?
A taxonomy code is a code that describes the provider or organization’s type, classification, and the area of specialization. You will find a complete list of taxonomy codes at www.wpc-edi.com/reference by selecting the Health Care Provider Taxonomy Code set link. The code set consists of two parts: individuals plus groups of individuals and non-individuals. An organizational NPI can have up to 15 taxonomy codes attached.

How do the NPI and taxonomy codes affect my billing?
NPIs for both the referring provider and the rendering provider must be on the claim for it to be processable by the insurance company. On the CMS 1500 form or the corresponding segment and loop on the 837P, the referring provider’s NPI is placed in Box 17b and the rendering provider’s NPI is placed in box 24j. The taxonomy code linked to the NPI of the rendering provider is used to verify the type of claims the practice can submit. For example, a practice with a taxonomy code of 207RH0003X (Hematology & Oncology) would not be able to submit a laboratory claim that falls under taxonomy code 29IU00000X (Clinical Medical Laboratories). Each NPI can have up to 15 taxonomy codes linked. If the practice has both taxonomy codes 207RH0003X and 29IU00000X linked to their NPI, the laboratory claim would be accepted. In this case, the practice would be a considered a multi-specialty group.

Can I change the taxonomy codes linked to the NPI?
Yes, your NPI can be edited and more taxonomy codes linked. If a provider with a different taxonomy code is added to the practice, you can edit your taxonomy code list. You cannot edit the primary taxonomy code, however. Go to https://nppes.cms.hhs.gov/#/ and log in to edit the record. Specific instructions are available from NanoString Technologies.
What if other information about the practice has changed?

Can that be edited?
Yes, you can make other edits to the NPI record by going to [https://nppes.cms.hhs.gov/#/](https://nppes.cms.hhs.gov/#/) and logging in to the NPI record. The NPI rules state that demographic changes should be made within 30 days of the change.

Can a provider or group have multiple NPIs?
Yes, there can be multiple NPIs associated with a provider. The provider will have an individual NPI (usually obtained during their medical training) and the provider may be associated with a group NPI. This association does not happen at NPPES, but rather through CMS form 855R or other insurance credentialing. If the physician is associated with a group, the group NPI should always be used for billing purposes.

Can an NPI be deactivated?
Yes. If a health care provider (for example, a physician) dies, his/her individual NPI will be deactivated. If a provider goes out of business, the individual NPI will also be deactivated. The deactivated NPI will never be issued to other health care providers. Movement of a provider from one geographical area of the country to another will not affect his/her NPI. However, if a provider is part of a group practice that bills using a Type 2 organizational number, that number will change if the provider leaves a group to join another group.

Helpful links:

The NPPES website can be used to create a new NPI, edit an existing NPI, or as a look-up for NPIs.

The Washington Publishing Company website. All HIPPA mandated code sets are found here, including a listing of taxonomy numbers.

[1-800-465-3203](tel:+18004653203)
NPPES customer service line can answer questions and provide assistance during the NPI application or edit process. They can also assist with forgotten user IDs or passwords.
How to Create a New Organizational NPI

Log in to NPPES ([https://nppes.cms.hhs.gov](https://nppes.cms.hhs.gov))

Create a New Account

You need an Identity and Access (I&A) Management System user ID and password to create and manage NPIs. If you do not have an I&A account or if you need to modify your I&A profile or gain access to a provider, click the CREATE or MANAGE AN ACCOUNT button to navigate to I&A.

Registered User Sign In

For existing account users, log in to view/update National Provider Identifier (NPI) records. Enter your user ID and password in the provided space, then click Sign In.

Forgot User ID or Password

If you have forgotten your user ID and/or password, click FORGOT USER ID or PASSWORD? and you will navigate to I&A where you can select to either Retrieve Forgotten User ID or Reset Forgotten Password.

- If you enter an incorrect user ID and password combination three times, your user ID will be disabled.
- Please contact the NPI Enumerator at 1-800-465-3203 if your account is disabled.

Actions

The following action buttons are available to help you navigate the NPI. The availability of each function is based on the NPI status.

- A file logo - To expand and view all NPIs associated with the organizational provider
- A magnifying glass logo - To view the NPI
- A pencil logo - To edit the NPI
- A dumpster/trash can logo - To delete the in-progress NPI

Status Definitions

- Green - Active
- Orange - Active with a pending change
- Grey - Pending (with or without errors)
- Blue - In progress (NPI application is not complete and/or has not yet been submitted)
- Red - Rejected (NPI application denied)
- Pink - Deactivated (NPI application to deactivate NPI has been approved NPI is currently inactive)

Manage Account and Provider Access

Select the Manage Account and Provider Access button to navigate to the I&A Management System. Select this button if you need to do any of the following functions:

- Update your User Profile
- Manage access to your provider’s NPI(s)
- Request access to a provider’s NPI(s)

Manage Provider Information

Providers will be listed in a grid, and users will have access to the NPIs associated with them. You may select a provider to view or modify an NPI. If the provider is associated with more than one NPI, select the file icon in the Action column to expand the provider and view all NPIs associated with that provider.

Use the search drop-down option to search for a provider. You can filter by any information displayed in the grid such as the provider’s name or address. You may also filter by status, using the drop-down option provided. Searchable status options are as follows:

- Active
- In Process
- Pending
- Rejected
- Pending Change Request
- In Progress Change Request

My Provider Information Grid

Provider information is listed in a grid format and provides the following information:

- Individual
- Organization
- Tax Identifier Number (TIN)
• Employer Identification Number (EIN)
• Social Security Number (SSN)
• Individual Taxpayer Identification Number (ITIN)
• Legal Business Name (LBN)
• Primary Practice Location
• NPI

When the provider organization has more than one NPI associated with it, “Multiple NPIs” will appear. Otherwise, this column will contain the NPI number if only one NPI is associated with the provider.

Apply for NPI
Click on Apply for an NPI for an Organization if you are applying for an NPI for an organization that renders health care services or a group practice or furnishes health care supplies to patients. The system will display a popup window asking you to identify whether you are applying for an NPI as an employee of the provider or a surrogate for the provider.

• As an employee of the provider: Upon selecting this button, you navigate to the Provider Profile page.
• As a surrogate working on behalf of the provider: Upon selecting this button, the system will ask you to identify which one of your employers is the surrogate organization. Upon selecting the employer, you will navigate to Provider Profile page.

Application Sections
There are 8 pages to the application. Each section is detailed below:
• Organizational Provider Profile
• Address
• Other Identifiers
• Taxonomy
• Contact Information
• Error Checking
• Submission
• Submission Confirmation

1. ORGANIZATIONAL PROVIDER PROFILE PAGE
The Organizational Provider Profile page captures the organization profile information associated with a Type 2 NPI.

Employer Identification Number (EIN)
The Health Insurance Portability & Accountability Act of 1996 (HIPAA) requires that employers have standard national numbers that identify them on standard transactions. The Employer Identification Number (EIN) is issued by the Internal Revenue Service (IRS) to identify a business entity. SSNs should never be reported in the EIN field.

Organization Name (Legal Business Name)
Provide the full legal business name of the organization. This name must match the one that the IRS has on file for the EIN. This is a required field and indicated with a red asterisk. If the provider organization’s EIN is already in NPPES, you will can select the legal business name from a dropdown list. If the provider organization’s EIN is not in the system, you will be required to enter the legal business name.

Is the Organization a subpart?
You are required to identify whether the organization is a subpart. If the organization is subpart of another organization, then select Yes. If the organization is not a subpart of another organization, then select No.

Is the parent EIN the same as the subpart EIN?
If you selected Yes indicating the provider organization is a subpart, the system will ask you if the provider organization’s EIN is the same as the parent organization’s EIN. Select Yes if the EINs are the same, or select No if the EINs are different. If you selected No indicating the parent EIN is different from the provider organization, you will be required to enter the parent organization’s EIN and legal business name. If the parent EIN is already in NPPES, you can select the appropriate legal business name from a dropdown list. If the parent EIN is not in NPPES, you will be required to enter the parent organization’s legal business name.
Other Organization Names
If your organization uses, or previously used, another name, supply those other names here. This information is not required. You can enter one or more additional names in this field. Select the Type of Other Name from the dropdown list.

Organizational Other Names Grid and Navigation
Upon selecting the Clear button the information populated in the Other Name fields will be cleared. Upon selecting the Save button, information populated in the Other Name fields will be saved to the grid.

Authorized Official for the Organization
An authorized official is an appointed official with the legal authority to make changes and/or updates to the provider’s status (e.g., change of address, etc.) and to commit the provider to fully abide by the laws and regulations relating to the NPI. The authorized official must be a general partner, chairman of the board, chief financial officer, chief executive officer, direct owner of 5 percent or more of the provider being enumerated, or must hold a position of similar status and authority within the provider organization.

Enter the following information for the authorized official:
- Prefix
- First Name
- Middle Name (Optional)
- Last Name
- Suffix
- Credential(s) (M.D, D.O, etc.)
- Title/Position
- Telephone Number
- Telephone Extension (if applicable)

2. ADDRESS PAGE
The address information will be used to contact the provider if there are any questions about the NPI application. You will be required to enter a business mailing address and a primary practice location. You may also enter multiple additional practice locations.

Business Mailing Address
You must provide an address where you can be contacted to resolve any issues or questions that may arise during review of your application or with other information regarding NPI.

Add a Business Mailing Address
Upon selecting Add a Business Mailing Address, you will navigate to the Business Mailing Address page. The following check box options are provided to select the practice location address type. The address type will be defaulted to US Domestic.
- US Domestic
- Military
- Outside US/Foreign

These check boxes will be available if no business mailing address has been associated with the NPI. The options will no longer appear once an address has been associated with the NPI.

Edit Business Mailing Address
Upon selecting Edit Business Mailing Address, you will navigate to the Business Mailing Address window where you can edit your business mailing address. This button will not appear until the business mailing address has been created/saved.

This is My Home Address
A check box is provided to specify if the address provided is same as the provider’s home address.

Business Mailing Address—US Domestic
Upon selecting US Domestic as a type of address, the business mailing address changes to accommodate the required address details and contact information. The Address Line 1, Address Line 2, and City fields allow the following special characters: ampersand, apostrophe, colon, comma, forward slash, hyphen, left and right parentheses, period, pound sign, quotation mark, and semi-colon. In addition, the Address Line 1 and Address Line 2 fields allow
the “at” sign. A field cannot contain all special characters.

• Address Line 1 – Enter line 1 of the mailing address here by typing in the street number and name in the given space.
• Address Line 2 (Optional) – Enter line 2 of the mailing address in the given space.
• City – Enter the name of the city.
• State - Select the state from drop-down list.
• Zip Code - Enter the zip code of the mailing address here.
• +4 Zip Code (Optional) – Enter the +4 zip code of the mailing address here.
• Telephone Number - Enter the telephone number here.
• Telephone Number Extension (Optional) – Enter the telephone number extension if applicable.
• Fax Number (Optional) – Enter the fax number if available.

Business Mailing Address — Military
Upon selecting Military as a type of address, the business mailing address changes to accommodate the required address details and contact information. Mailing address Line 1, Mailing Address Line 2, and City fields allow the following special characters: ampersand, apostrophe, colon, comma, forward slash, hyphen, left and right parentheses, period, pound sign, quotation mark, and semi-colon. In addition, the Address Line 1 and Address Line 2 fields allow the “at” sign. A field cannot contain all special characters.

• Address Line 1 – Enter line 1 of the mailing address here by typing in information such as the PSC or ship name in the given space.
• Address Line 2 (Optional) – Enter line 2 of the mailing address here by typing in information such as the CVN, box number, or unit number in the given space.
• City – Select the city from the drop-down list. The list of choices given are APO, FPO, and DPO.
• State – Select the state from the drop-down list. The list of choices given are AA, AE, AP.
• Zip Code – Enter the zip code here.
• +4 Zip Code (Optional) – Enter the +4 zip code.
• Telephone Number – Enter the telephone number here.

Business Mailing Address — Outside US/ Foreign
Upon selecting Outside US/ Foreign as a type of address, the business mailing address changes to accommodate the required address details and contact information. Address Line 1, Address Line 2, and City fields allow the following special characters: ampersand, apostrophe, colon, comma, forward slash, hyphen, left and right parentheses, period, pound sign, quotation mark, and semi-colon. In addition, the Address Line 1 and Address Line 2 fields allow the “at” sign. A field cannot contain all special characters.

• Address Line 1 – Enter line 1 of the mailing address here by typing in the street number and name in the given space.
• Address Line 2 (Optional) – Enter line 2 of the mailing address here by typing in the suite number and any other additional address information in the given space.
• City – Enter the name of the city in the given space.
• Province or Territory – Enter the foreign province name or territory name in the given space.
• Postal Code – Enter the foreign postal code in the given space.
• Country – Select the name of the country from the drop-down list.
• Telephone Number – Enter the telephone number associated with the mailing address.
• Extension (Optional) – Enter the telephone number extension if applicable.
• Fax Number – (Optional) Enter fax number if available.

Business Mailing Address Window Navigation
Upon selecting the Clear, the information populated in the provided spaces will be cleared. Upon selecting Save, information populated in the provided spaces will be saved.
**Practice Location Address**

You must provide a physical address; this cannot be a P.O. Box. This address should be the location where the actual services are rendered. Users can enter multiple addresses, but only one primary practice location is required.

**Add a Practice Location**

Upon selecting Add a Business Practice Location, you will be navigated to the Practice Location Address window where you can enter the practice location address information. This button will be available if no practice location address has been associated with the NPI. The button will no longer appear once a practice location address has been associated with the NPI.

**Add Another Practice Location**

Upon selecting Add another Practice Location, you will be navigated to Practice Location Address page where you can enter a new practice location to associate with the NPI.

**Practice Location Address Window**

Practice Location Address page identifies the address(es) where service is rendered. You may associate multiple practice locations with an NPI, however, at least one practice location must be associated with an NPI and one practice location must be identified as the primary practice location.

**Select Type of Practice Location Address**

The following options are provided to select the practice location address type. The address type will be defaulted to US Domestic.

- US Domestic
- Military
- Outside US/Foreign

**Practice Location is the Same as Mailing Address**

A check box is provided to specify if the practice location address is same as the business mailing address. When selected, the address will be pre-populated with the business mailing address information.

**This is My Home Address**

A check box is provided to specify if the practice location address being provided is the same as the provider’s home address.

**Primary Practice Location Address**

A check box is provided to specify if the address provided is the primary practice location address.

**Practice Location—US Domestic**

Upon selecting US Domestic, the practice location page changes to accommodate the required address details and contact information. The Practice Location Address Line 1, Address Line 2, and City fields allow the following special characters: ampersand, apostrophe, colon, comma, forward slash, hyphen, left and right parentheses, period, pound sign, quotation mark, and semi-colon. In addition, the Address Line 1 and Address Line 2 fields allow the “at” sign. A field cannot contain all special characters.

- Address Line 1 – Enter line 1 of the mailing address here by typing in the street number and name in the given space.
- Address Line 2 (Optional) – Enter line 2 of the mailing address in the given space.
- City – Enter the name of the city by typing in the given space.
- State – Select the state from drop-down list.
- Zip Code – Enter the zip code.
- +4 Zip Code (Optional) – Enter the +4 zip code.
- Telephone Number – Enter the telephone number.
- Extension (Optional) – Enter the telephone number extension if applicable.
- Fax Number (Optional) – Enter the fax number if available.

**Practice Location Address—Military**

Upon selecting Military, the practice location address changes to accommodate the required address details and contact information. The Practice Location Address Line 1, Address Line 2, and City fields allow the following special
characters: ampersand, apostrophe, colon, comma, forward slash, hyphen, left and right parentheses, period, pound sign, quotation mark, and semi-colon. In addition, the Address Line 1 and Address Line 2 fields allow the “at” sign. A field cannot contain all special characters.

• Address Line 1 – Enter line 1 of the mailing address here by typing in information such as the PSC or ship name in the given space.
• Address Line 2 (Optional) – Enter line 2 of the mailing address here by typing in information such as the CVN, box number, or unit number in the given space.
• City – Select the city from the drop-down list, this is a mandatory field. The list of choices given are APO, FPO, and DPO.
• State – Select the state from the drop-down list. The list of choices given are AA, AE, AP.
• Zip Code – Enter the zip code here.
• +4 Zip Code (Optional) – Enter the +4 Zip Code.
• Telephone Number – Enter the telephone number here.
• Telephone Number Extension (Optional) – Enter telephone number extension if applicable.
• Fax Number (Optional) – Enter fax number if available.

Languages Spoken
Providing the languages spoken at a practice location is optional. You may select one or more languages.

Office Hours
Providing the office hours of a practice location is optional. Specify office hours and timing details as follows:
• Seven sliding buttons with options to select Open or Closed are provided for each day of the week starting from Monday to Sunday.
• Under each day there are two drop-down boxes to indicate the opening and closing times.
• A check box option is provided to select or deselect ‘apply to all’. By selecting the check box, the times indicated in the two drop-down boxes will be applied to all the days that are selected as Open.

Accessibility
Providing the practice location’s accessibility to individuals with mobility disabilities is optional.
• Identify if the practice location office is accessible to individuals with mobility disabilities by selecting the appropriate option, Yes or No.
• Identify if the practice location office exam rooms are accessible to individual with mobility disabilities by selecting the appropriate option, Yes or No.
• Identify if the practice location office medical equipment is accessible to individual with mobility disabilities by selecting the appropriate option, Yes or No.

Practice Location Address—Outside US/ Foreign
Upon selecting Outside US/ Foreign, the mailing address changes to accommodate the required address details and contact information. The Practice Location Address Line 1, Address Line 2, and City fields allow the following special characters: ampersand, apostrophe, colon, comma, forward slash, hyphen, left and right parentheses, period, pound sign, quotation mark, and semi-colon. In addition, the Address Line 1 and Address Line 2 fields allow the “at” sign. A field cannot contain all special characters.

• Address Line 1 – Enter line 1 of the mailing address here by typing in the street number and name in the given space.
• Address Line 2 (Optional) – Enter line 2 of the mailing address here by typing in the suite number and any other additional address information.
• City – Enter the name of the city in the given space.
• Province or Territory – Enter foreign province name or territory name in the given space.
• Postal Code – Enter the foreign postal code in the given space.
• Country – Select the name of the country form the drop-down list.
• Telephone Number – Enter the telephone number associated with the mailing address.
• Extension (Optional) – Enter the telephone number extension if applicable.
• Fax Number (Optional) – Enter fax number if available.
3. OTHER IDENTIFIERS PAGE

The Other Identifiers page is used to associate a provider’s identifiers with their NPI. NPPES collects both endpoints and identifiers assigned to providers by health insurers and Medicaid.

Endpoint (Optional)

Associating endpoints with an NPI is optional. If you wish to enter an endpoint, please fill in the required data. You can learn more about direct addresses and endpoints by selecting the links provided on the page.

Endpoint Type

When entering an endpoint, you are required to enter the endpoint type. Select the Endpoint Type using the dropdown list with the following options:
- Direct Address
- Regular Email Address
- SOAP URL
- Connect URL
- FHIR URL
- Restful URL
- Website URL
- Other URL

Endpoint

When entering an endpoint, you are required to enter the actual endpoint. If you are entering a direct address or regular email address, you will be required to enter a well-formatted email address.

Is the provider affiliated to another organization?

When entering an endpoint, you are required to identify whether it is to affiliate the provider to another organization by selecting the appropriate button, Yes or No.
- Affiliation Type: If you selected Yes, identifying the provider to be affiliated with another organization, you will be required to identify the Affiliation ID.
- If you selected the Affiliation Type as NPI, enter the organization’s NPI in the Affiliation ID. If you need help finding the NPI, select the Search NPI Registry link at the top right hand corner of the page to search for the organization’s NPI.
- If you selected the Affiliation Type of EIN, enter the organization’s EIN in the Affiliation ID.

Endpoint Grid

The endpoint grid allows you to see all endpoints that have been associated with the NPI. You can filter the endpoints that display in the grid by searching for data from any column. For example, if you search for ‘Tom’, all endpoints that contain the word ‘Tom’ (not case sensitive) will be displayed in the grid. The results would show endpoints with ‘Tomas’, ‘Tom’, and ‘bottom’. If you wish to delete an endpoint, select the trash can icon in the Actions column.

Endpoint Navigation

The following are navigation buttons provided at the bottom of the Endpoint section on the Other Identifiers page:
- Upon selecting Clear, the information populated in the provided spaces will be cleared.
- Upon selecting Save, information populated in the provided spaces will be saved.

Other Identifiers (Optional)

Associating other provider identifiers with an NPI is optional. This information is publicly disseminated, so you should not enter personal identifiable information (PII) such as Social Security Number (SSN), IRS Individual Taxpayer Identification Number (ITIN), or Employer Identification Number (EIN) in this section. DO NOT report Medicare identifiers in this section. These numbers will be used to match your NPI record to insurer’s records so you can continue to be recognized by insurers. If you don’t have such numbers, you are not required to obtain them. Legacy
numbers may be entered in the Other Provider Identifiers section of the National Provider Identifier (NPI) application. The NPI Enumerator encourages providers to provide this information, but if you are in doubt about whether to include them on your NPI application, please contact the health plans with which you conduct business for clarification. You may submit a maximum of 50 other provider identifiers with an NPI.

Issuer
Identify the issuer of the other identifier that you are entering. Select the MEDICAID to enter your Medicaid Identification Number. Select Other, Specify to enter an identifier associated with a health plan other than Medicaid or Medicare (e.g., Blue Cross, Blue Shield, Aetna, Kaiser-Permanente, etc.). When selecting another identifier, the name of the health plan that is assigned the identifier must be entered.

Identification Number
Enter the identification number associated with the issuer you have selected.

State Issued (If Applicable)
Select the state from the drop-down box that is associated with the other identifier specified, if applicable.

Other Identifiers Grid
The Other Identifiers grid allows you to see all other identifiers that have been associated with the NPI. You can sort the grid by issuer or state. If you wish to delete an entry, select the trash can icon in the Actions column.

Other Identifier Navigation
The following are the other navigation buttons provided at the bottom of the Other Identifier section on the Other Identifiers page:

- Upon selecting Clear, the information populated in the provided spaces will be cleared.
- Upon selecting Save, information populated in the provided spaces will be saved.

4. TAXONOMY PAGE
A taxonomy code is a code that describes the provider or organization's type, classification, and the area of specialization. You will find a complete list of taxonomy codes at [www.wpc-edi.com/reference](http://www.wpc-edi.com/reference) by selecting Health Care Provider Taxonomy Code Set link. The code set consists of two parts: individuals plus groups of individuals and non-individuals.

You are required to identify at least one taxonomy to associate with your NPI. If you identify more than one, you must identify which one is the primary taxonomy. Provider taxonomy codes and their description can be found on the Washington Publishing Company’s web page at [http://www.wpc.edi.com/codes/taxonomy](http://www.wpc.edi.com/codes/taxonomy)

To enter a taxonomy code, start by entering either the taxonomy code, classification code, or specialty in the search box. All taxonomies containing the data you enter will display, allowing you to select the appropriate one. Once you have selected the appropriate taxonomy code, select the Add Taxonomy button to populate the corresponding fields below the search box. Complete your taxonomy code entry by entering the license and state information.

Practice Type
Identify the type of practice by selecting from the following options:

- Not a Group - Not a group
- Multi-Specialty Group - Groups having members with more than one taxonomy
- Single-Specialty Group - Groups having members with one taxonomy
- Multiple Single Specialty - Groups having more than one location and the members have one taxonomy

Taxonomy Code Search Box
Enter any part of the taxonomy, the taxonomy number, classification code, or specialty in the search box. The system will then display all taxonomies containing the
information you entered. Select the desired taxonomy to populate the taxonomy fields.

**Provider Type Code**
This field will be populated based on the taxonomy you select in the taxonomy search box.

**Classification Name/Specialization**
This field will be populated based on the taxonomy you select in the taxonomy search box.

**License Number**
Enter the license number associated with the taxonomy, if applicable. Some taxonomies require a license, and the system will prompt you if one is required.

**State Issued**
Select the two-digit state code to identify the license issued by the state, when applicable.

**Taxonomy Grid**
The taxonomy grid allows you to see all taxonomies that have been associated with the NPI. You can filter the list of displayed taxonomies by entering taxonomy data from any column in the grid. If you wish to delete a taxonomy, select the trash can icon in the Actions column.

5. CONTACT INFORMATION PAGE
**Contact Person Information**
The contact person is the person who will be contacted if there are any questions regarding your NPI application or change request. This is the person who will be notified of your NPI assignment via the e-mail address provided on this page.

**Contact Person Is Same as Authorized Official**
If you are creating a Type 2 NPI and the contact person is the same as the authorized official, then select the button that indicates Contact Person is same as the Authorized Official. This selection will populate the contact person name with the authorized official’s name entered on the Provider Profile page.

**Contact Person Is Same as Myself**
If the contact person is yourself, then please select the button that indicates Contact Person is same as Myself. Selecting this button will populate the contact person information with your information from your I&A account.

**Contact Person Name and Contact Information**
Provide the following information for the contact person:
- Prefix - Select the appropriate name prefix from the dropdown list.
- First Name - Provide the first name of the authorized official. This is a mandatory field.
- Middle Name - Provide the middle name of the authorized official. This field is optional.
- Last Name - Provide the last name of the authorized official. This is a mandatory field.
- Suffix - Select the authorized official’s name suffix from the dropdown list, if applicable.
- Credential(s): (M.D, D.O, etc.) - Providing the authorized official’s credentials is optional.
- Title/Position - Provide the title and or position of the authorized official. This is a mandatory field.
- Telephone Number - Provide the telephone number. This is a mandatory field.
- Extension - Provide telephone number extension, if applicable.

6. ERROR CHECK PAGE
This page provides you with the status of your NPI application. You must resolve all errors before you can submit your NPI application. If the information provided in any step is incorrect, the page will identify all errors associated with that step. If the information provided is
correct and complete, the page will indicate that no errors were found.

For each step, a separate button will take you to that location in the application so that you may review and modify the information. If there are no errors, the button will say Review. If there are any errors, the button will say Update.

**Step 1: Provider Profile**
If any errors were found with the information entered on the Provider Profile page, they will be indicated here, otherwise the status will display as GOOD. The Update button will be available if errors were found in the provider profile data entered. The Review button will be available if there are no errors associated with the provider profile. Selecting either Update or Review will navigate you to the provider profile information.

**Step 2: Business Mailing Address**
The Update button will be available if errors were found in the business mailing address entered. The Review button will be available if there are no errors associated with this page. Selecting either Update or Review will navigate you to the Business Mailing Address page.

**Step 3: Other Identifiers**
The Update button will be available if errors were found in the other identifiers entered. The Review button will be available if there are no errors associated with this page. Selecting either Update or Review will navigate you to the Other Identifiers page.

**Step 4: Taxonomy**
The Update button will be available if errors were found in the taxonomy entered. The Review button will be available if there are no errors associated with this page. Selecting either Update or Review will navigate you to the Taxonomy page.

**Step 5: Contact Information**
The Update button will be available if errors were found in the contact information entered. The Review button will be available if there are no errors associated with this page. Selecting either Update or Review will navigate you to the Contact Information page.

**7. SUBMISSION PAGE**
Under the Submission Certification section, you are required to accept the following statements before submitting the application:

- I have read the contents of the supplication and the information contained herein is true, correct, and complete. If I become aware that any information in this application is not true, correct or complete, I agree to notify the NPI, enumerator of this fact immediately.
- I authorize the NMPI Enumerator to verify the information contained herein. I agree to keep the NPPES updated with any changes to data listed on this application form within 30 days of the effective date of the change.
- I have read and understood the Privacy Act Statement.

**Penalties for Falsifying Information**
18 U.S.C. 1001 authorizes criminal penalties against an individual who in any matter within the jurisdiction of any department or agency of the United States knowingly or willfully falsifies, conceals, or covers up by any trick, scheme or device a material fact, or makes any false, fictitious or fraudulent statements or representations, or makes any false writing or document knowing the same to contain any false, fictitious or fraudulent statement or entry.

Individual offenders are subject to fines of up to $250,000 and imprisonment for up to five years. Offenders that are organizations are subject to fines of up to $500,000. 18 U.S.C. 3571(d) also authorizes fines of up to twice the gross gain derived by the offender if it is greater than the amount specifically authorized by the sentencing.
Certify Check Box
This section contains a check box stating that “I certify that this form is being completed by, or on behalf of, a health care provider as defined at 45 CFR 160.103”. This is a mandatory field. Upon selecting this check box, the Submit button becomes activated, otherwise it is greyed out.

Privacy Act Statement Hyperlink
Upon selecting the Privacy Act Statement link you will be navigated to the Privacy Act Statement page.

Submit Button
The Submit button is greyed out and is not activated until you select the check box that indicates “I certify that this form is being completed by, or on behalf of, a health care provider as defined at 45 CFR 160.103”. Upon selecting the Submit button you will navigate to the Submission Confirmation page.

8. SUBMISSION CONFIRMATION PAGE
Submission Confirmation for a Type 2 NPI
Upon selecting the Submit button from the Submission Certification page, you will navigate to the Submission Confirmation page where you will see the following statement:

“Thank You. Your application will be processed. Your tracking number is: XXXX. If you have any questions regarding this application or if the designated contact person did not receive the provider’s NPI via email within 15 working days, please refer to the FAQ Menu. To learn more click here. You have successfully submitted your NPI application for: * Organization Name: XXXX * Authorized Official: XXXX * Contact Person: XXXX * Primary Practice Location Address: XXXX * EIN: 99-9999999 * Primary Taxonomy / Specialty: XXXX * Date Submitted: XXXX * Contact Email: XXXX An email confirmation has been sent to the contact person listed on this application NPI Enumerator contact information By Phone: 1-800-465-3203 (NPI Toll-Free) 1-800-692-2326 (NPI TTY) By e-mail at: customerservice@npienumerator.com By mail at: NPI Enumerator PO Box 6059 Fargo, ND 58108-6059”

Submission Confirmation Page Navigation
Two buttons are provided on the Submission Confirmation page:
• Print this Page - Navigates to the printer setup page to select the printer to print the page.
• View Printer Friendly Version of Application Button - You will be provided with a printer friendly version in Adobe Acrobat format to view before you print.

Adding an Additional Taxonomy to Your NPI
Updates can be made online by accessing https://nppes.cms.hhs.gov and completing the steps below:

Step 1: Log in to https://nppes.cms.hhs.gov
Enter your I&A user ID and password on the home page of the NPPES website.

Step 2: Select the Magnifying Glass icon to view the desired NPI application

Step 3: Select the Pencil icon to edit the desired NPI application
To access the page that contains the information to be updated, select the Next button located at the bottom of each page or by selecting the desired page from the left-hand navigation bar.

Step 4: Navigate to the Taxonomy page by either:
• Selecting Taxonomy from the left navigation panel.
• Selecting Taxonomy on the top progression bar.
• Selecting Next until you are navigated to the Taxonomy page.

Step 5: To add a taxonomy code
• Select Add Taxonomy.
• Select 291U00000X Clinical Medical Laboratory.
• Input an associated license and state of issue, if applicable.
• Select Save to store the new information and return to a list of all taxonomy and licenses currently on the record.

**Step 6: Submit Changes**

• Once all desired information is updated, navigate to the Submission page. Check the Certification Statement box at the bottom of the page.
• Select Submit. This button will not be enabled until you check the Certification Statement box at the bottom of the page.

**Additional Notes**

If you do not have the user ID and/or password, follow the instructions found on the website. If you continue to have issues accessing your NPI(s), contact the NPI Enumerator at 800-465-3203 for further assistance. Please be aware that there are privacy guidelines that govern to whom the NPI Enumerator can disclose information.

Once you have added the taxonomy for Clinical Medical Laboratories 291U00000X, you will be prompted to change your provider type. Change this from Single Specialty to Multi-Specialty.

**Overview of MolDx and the Z-Code Identifier**

*What is the MolDx program?*

The MolDx program is a CMS program to help identify and monitor Molecular Diagnostic Laboratory tests. Established in 2011, the program is administered by Palmetto GBA and currently covers CMS jurisdictions JE, JF, JJ, JM, J15, J5, and J8, which includes the states below.

*How does MolDx identify and monitor the tests?*

The MolDx program partnered with the McKesson Diagnostic Exchange to help create a unique identifier to identify these tests. Each laboratory that runs a test meeting the MolDx criteria and that is in a MolDx state must register with the McKesson Diagnostic Exchange. Once registered, the laboratory must submit an application for a Z-code identifier. Once a Z-code identifier is issued, the laboratory and the test are listed in the McKesson Diagnostic Exchange catalog. The Z-code identifier and the CPT code for the test are then linked in the CMS system to make adjudication of these claim faster and more accurate.

*What information does the McKesson Diagnostic Exchange collect?*

McKesson Diagnostic Exchange collects demographic information about the laboratory, including NPI and CLIA license information. As part of the Z-code identifier application, information about the molecular components of a test, methodology used to conduct the test, and the medical indications for the test are collected. You can also provide information about the test’s clinical validity, analytical sensitivity, and specificity. This information is optional.
**Do I need a Z-code if I am running a kit from a manufacturer that already has a Z-code identifier?**
You must register and apply for a Z-code identifier if you are billing for a molecular diagnostic test. If you are using an unmodified FDA-approved kit, you will be assigned the same Z-code identifier as the manufacturer. If you bill for the test using the manufacturer’s Z-code identifier without registering and applying for a Z-code, your claims will be denied. Once you have been issued a Z-code identifier, you can bill Medicare and get paid for the test so long as coverage guidelines are met. If you are modifying an FDA-approved kit, you will be assigned a unique Z-code identifier because the modification creates a proprietary test. This means that existing coverage guidelines may not apply to your test and your claim may be denied.

**How do I know if I need a Z-code identifier?**
Z-code identifiers are needed if your lab is in one of the jurisdictions listed above and you are billing one of the following CPT codes:

**Are Z-code identifiers used by any insurances other than Medicare?**
Currently there are four commercial insurances requiring a Z-code identifier to adjudicate claims. They are Medical Mutual of Ohio, Paramount, Fallon, and Independent. This list may be added to at any time so if you have questions about the need for a Z-code, check with the insurance company or McKesson for an updated list.

**Where does the Z-code identifier go on the claim?**
- Loop 2400 or SV101-7 for the 5010A1 837P
- Box 19 for paper claim

**Helpful links:**
The MolDx program website: [http://www.palmettogba.com/palmetto/MolDX.nsf](http://www.palmettogba.com/palmetto/MolDX.nsf)
The McKesson Diagnostic Exchange website, where you can register and apply for a Z-code identifier: [https://app.dexzcodes.com](https://app.dexzcodes.com)

<table>
<thead>
<tr>
<th>Code Category/Description</th>
<th>2017 MolDx Code Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tier 1</td>
<td>81161-81383</td>
</tr>
<tr>
<td>Tier 2</td>
<td>81400-81479</td>
</tr>
<tr>
<td>Genomic Sequencing and other MAA</td>
<td>81410-81471</td>
</tr>
<tr>
<td>Molecular Multianalyte Assays (MAA)</td>
<td>81410-81471</td>
</tr>
<tr>
<td>MAA</td>
<td>81490-81595</td>
</tr>
<tr>
<td>MAA Proprietary Codes</td>
<td>0001M-0009M</td>
</tr>
<tr>
<td>Immunology</td>
<td>86152-86153</td>
</tr>
<tr>
<td>Microbiology</td>
<td>87505-87507, 87631-87633, 87149-87150</td>
</tr>
<tr>
<td>PLA</td>
<td>*All Codes</td>
</tr>
<tr>
<td>HCPCS: Molecular pathology procedure; physician interpretation and report</td>
<td>G0452</td>
</tr>
<tr>
<td>NOC</td>
<td>81479, 81599, 84999, 85999, 86849, 87999, 88199, 88299, 88399, 89398</td>
</tr>
</tbody>
</table>
How to Register with McKesson Diagnostic Exchange

Step 1: Go to https://app.dexzcodes.com/login

Step 2: Click on Register as a Lab or Manufacturer
Step 3: Create the Organization

1. Choose your organization type – Lab
2. Choose laboratory type – Physician office laboratory
3. Complete the remainder of the Organization page.
   Fields with a red asterisk are required.
4. Click NEXT at the bottom of the page
**Step 4:** Enter the Contact Information

Enter the Laboratory Medical Director’s name. Only items with a red asterisk are required.
Step 5: Consent to Terms and Conditions
1. Review Terms and Conditions
2. Click Accept and Continue

Step 6: Consent to Terms and Conditions, Continued
Click Not Now at the bottom of the page
**Step 7: Participation**

1. This screen deals with the insurances that will accept technical assessment information through the McKesson Exchange. You must click at least 1 insurance to continue. Since you are not registering a proprietary test, this will not share any data.
2. Click NEXT at the bottom of the page.
**Step 8: Administrator Contact**

The administrator contact can manage and edit lab tests, users, coverage determinations and organizational/display settings as well as browse the catalog.

1. Enter email address of the administrator contact
2. Re-enter email address of the administrator contact
3. Enter administrator contact’s first name
4. Enter administrator contact’s last name
5. Enter administrator contact’s job title
6. Click NEXT at the bottom of the page
**Step 9: Assign a Clinical Resource**

The clinical resource and the administrator contact may be the same. However, the clinical resource must have a medical credential, such as MD or RN.

1. Indicate if the administrator contact and clinical resource are the same
2. Enter the clinical resource’s credentials
3. Enter the clinical resource’s name
4. Enter the clinical resource’s email
5. Re-enter clinical resource’s email
6. Click Finish at the bottom of the page

McKesson Diagnostic Exchange will then activate your registration, which may take several days. The administrator contact and clinical resource will receive an email from DEX, Customer.Service@changehealthcare.com, allowing them to set up their password. The username is the administrator contact’s email address.

The next step is submitting an application for a Z-code.
Adding the Prosigna Test to McKesson Diagnostic Exchange

Step 1: Log in. Go to https://app.dexzcodes.com/login

Log in with your username and password. The user ID is the email for the administrator or clinical resource added when registering for access to the McKesson Diagnostic Exchange. If you have not registered with the Exchange, please see the previous section in this document, How to Register with the McKesson Diagnostic Exchange. If you need help logging in, contact the Diagnostics Exchange Customer Service at DEX.Customer.Service@changehealthcare.com.

Step 2: Add a Test. Once you have logged in, click on the Add Test button:

Notes:

• All fields with a red asterisk must be completed. The text to complete the field is specified below unless otherwise noted.

• Always use the NEXT or BACK buttons to navigate to the previous or next page. Using your browser buttons will cause you to lose your work.

• At any time, you can save the application as a draft. Doing this will allow you to stop the process with all the input information saved.
Step 3: General Information. The first section of the application is for general information. This application must reflect the same information that has been provided by NanoString to the Exchange.

1. **Test ID** – This is your lab’s identifier for the Prosigna test

2. **Test Title** – Copy and paste or type:
   Prosigna® Breast Cancer Prognostic Gene Signature Assay

3. **Are you the Performing Lab?** – Check Yes
4. **Test Description** – Copy and paste or type the following text:
The Prosigna® breast cancer prognostic assay is an FDA 510(k)-cleared assay that provides a risk category and numerical score to assess a patient’s risk of distant recurrence of disease at 10 years in postmenopausal women with node-negative (Stage I or II) or node-positive (Stage II), hormone receptor-positive (HR+) breast cancer. The Prosigna® assay measures gene expression levels of RNA extracted from formalin-fixed paraffin-embedded (FFPE) breast tumor tissue previously diagnosed as invasive breast carcinoma.
5. **Molecular Component** – Copy and paste or type the following text:

ANLN, CCNE1, CDC20, CDC6, CDCA1, CENPF, CEP55, EXO1, KIF2C, KNTC2, MELK, MKI67, ORC6L, PTTG1, RRM2, TYMS, UBE2C, UBE2T, ACTR3B, BAG1, BCL2, BIRC5, BLVRA, CCNB1, CDH3, CXXC5, EGFR, ERBB2, ESRI, FGFR4, FOXA1, FOXC1, GPR160, GRB7, KRT14, KRT17, KRT5, MAPT, MDM2, MIA, MLPH, MMP11, MYBL2, MYC, NAT1, PGR, PHGDH, SFRP1, SLC39A6, TMEM45B, TFRC, GUSB, MRPL19, SF3A1, PSMC4, RPLP0, PUM1 and ACTB
6. **Variants/Mutations/Alleles/Loci Probes** – Copy and paste or type the following text:

ANLN - NM_018685.2; CCNE1 - NM_001238.1; CDC20 - NM_001255.1; CDC6 - NM_001254.3; CDCA1 - NM_145697.1; CENPF - NM_016343.3; CEP55 - NM_018131.3; EXO1 - NM_006027.3; KIF2C - NM_006845.2; KNTC2 - NM_006101.1; MELK - NM_014791.2; MKI67 - NM_002417.2; ORC6L - NM_014321.2; PTTG1 - NM_004219.2; RRM2 - NM_001034.1; TYMS - NM_001071.1; UBE2C - NM_007019.2; UBE2T - NM_014176.1; ACTR3B - NM_001040135.1; BAG1 - NM_004323.3; BCL2 - NM_000633.2; BIRC5 - NM_001168.2; BLVRA - NM_000712.3; CCNB1 - NM_031966.2; CDH3 - NM_001793.3; CXXC5 - NM_016463.5; EGFR - NM_005228.3; ERBB2 - NM_004448.2; ESR1 - NM_000125.2; FGFR4 - NM_002011.3; FOXA1 - NM_004496.2; FOXC1 - NM_001453.1; GPR160 - NM_014373.1; GRB7 - NM_005310.2; KRT14 - NM_000526.3; KRT17 - NM_000422.1; KRT5 - NM_000424.2; MAPT - NM_01835.3; MDM2 - NM_006878.2; MIA - NM_006533.1; MLPH - NM_024101.4; MMP11 - NM_005940.3; MYBL2 - NM_002466.2; MYC - NM_002467.3; NAT1 - NM_000662.4; PGR - NM_000926.2; PHGDH - NM_006623.2; SFRP1 - NM_003012.3; SLC39A6 - NM_012319.2; TMEM45B - NM_138788.3; TFRC - NM_003234.1; GUSB - NM_000181.1; MRPL19 - NM_014763.3; SF3A1 - NM_005877.4; PSMC4 - NM_006503.2; RPLP0 - NM_001002.3; PUM1 - NM_001020658.1 and ACTB - NM_001101.2

7. **Click NEXT**
**Step 4: Clinical Information**

1. FDA 510(k)/PMA – Click Yes
2. FDA document # - Copy and paste or type: K130010 K141771
3. Modification to FDA Cleared/Approved Protocols – Click No
4. Device/Kit – Click Yes
5. Device/Kit Manufacturer – Copy and paste or type:
   NanoString Technologies
6. Device/Kit Name – Copy and paste or type: Prosigna™
7. Click NEXT
Step 5: Categories

- In each section, you must select an entry from Column A and add it to Column B (See image below).
- Use the ADD and REMOVE buttons to navigate between the columns.
- To highlight a selection, click on it.
- Click ADD to move a highlighted selection to Column B.
- Click REMOVE to clear the highlighted selection from Column B.
- You can ADD multiple selections to Column B.

1. **Test Type**—In Column A, find Prognostic. Highlight it and click ADD.

2. **Disease/Disorders** – In Column A, find Breast Cancer, any type. Highlight it and click ADD.
3. **Methodology** - In Column A, find nCounter® DX Analysis System. Highlight it and click ADD.

4. **Medical Specialties** - In Column A, find your group’s Specialty. Highlight it and click ADD.
5. **FDA** – In Column A, select FDA501(k) cleared. Highlight it and click ADD.

6. Medical Specialties and FDA are not required fields and they can be left blank.

7. **Click NEXT.**

---

**Step 6: Financial Information**

1. Add CPT® codes (Current) – Type 81520. A drop-down box will appear. Choose 81520 from the drop-down.

2. A pop-up box will appear for the CPT Units. Enter 1 in the box and click ADD.

3. The rest of the fields on this page are not required and may be left blank.

4. Click NEXT.
Step 7: Advanced

1. Algorithm – Click NO
2. Comparable Test/Assay – leave blank
3. Specimen Information – Copy and paste or type:
   Formalin-fixed, paraffin-embedded (FFPE) tissue block or slides.

4. None of the other fields on Advanced tab are required.
5. If you have missed a required field or entered information in the wrong format, you will see a red popup window locating the error. You can save a draft with errors but you cannot submit an application with errors. Once any errors are corrected, click the Review and Submit button.
Once you have submitted, the application is locked and cannot be edited. The McKesson Diagnostic Exchange may come back to you with questions about your application. If this happens, please contact NanoString Technologies for assistance.

It can take up to 30 business days for your Z-code to be assigned by the Exchange. Once the Z-code is assigned, the two users registered with the Exchange will be notified by email. If you do not receive an email within 30 business days, you can reach out to the Exchange at DEX.CustomerService@changehealthcare.com

For more information please visit prosigna.com