

*2017 Update*

# The Current Landscape of Genetic Testing

An up-to-date overview of market size,  
market growth, and the practical challenges  
of the clinical workflow

March 2017

# EXECUTIVE SUMMARY

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This is the 2017 edition of a report first released in 2016. It is intended to present the current landscape of clinical genetic diagnostics in the United States. Concert Genetics is a health IT company leveraging data science and technology to track the genetic diagnostics market and provide the digital infrastructure for reliable and efficient management of genetic testing.

## Key points addressed in this document include:

### 1. Market Size

There are almost 70,000 genetic testing products on the US market.

### 2. Market Growth

An average of approximately 10 new testing products enter the market every day, making it difficult for stakeholders across the healthcare system to manage the pace of change.

### 3. Next Generation Sequencing

Much of the growth in the market is attributable to NextGen Sequencing (NGS), which now accounts for an estimated 48% of the tests currently on the market.

### 4. Complexity and Variety

Testing options are becoming more complex, with laboratories packaging testing products in a widening variety of ways. *BRCA1/2*, Exome and Non-invasive Prenatal Testing (NIPT), specifically, are available in increasing variety.

### 5. Clinical Workflow

Healthcare providers face mounting challenges integrating genetic testing into the clinical workflow. Utilization management tools, such as the Concert Platform, are helping institutions across the country address and overcome these challenges.

We hope that the data in this document, and the tools we've built to address these challenges, will be helpful to stakeholders across the healthcare system as they work together to deliver on the promise of precision medicine.

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Nick Tazik at [ntazik@concertgenetics.com](mailto:ntazik@concertgenetics.com)*

# 1. MARKET SIZE

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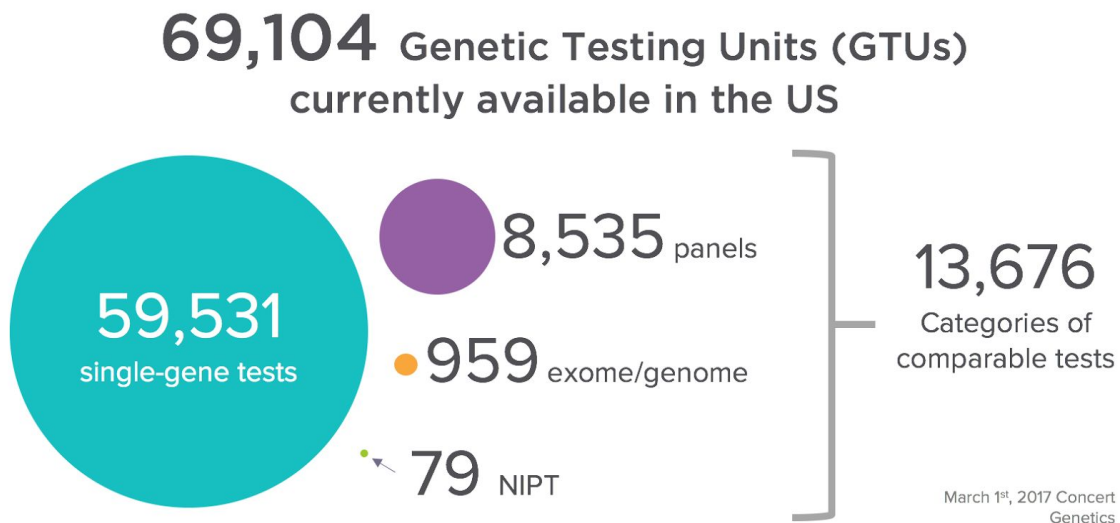
How many genetic diagnostic test products are currently marketed by CLIA-certified laboratories in the United States?

## A. Total Testing Products on the Market

Concert Genetics has collected information on 69,104 **Genetic Testing Units (GTUs)** that are active and available for ordering as of March 2017. In our database, a GTU is a unique orderable combination of analytes (i.e., genes or other targets) and techniques at a specific point in time, sold by a laboratory as a single item in the laboratory's catalog.

Stated another way, a GTU (elsewhere referred to as a "testing product") is a usually equivalent to a checkbox on a lab requisition form. Currently, there are at least 69,104 of them.

Of these, 59,531 assay a single gene or analyte. 8,535 are panels that assay multiple genes or analytes for a common indication, and each panel is sold as a single orderable unit with its own test code in a laboratory's catalog. A total of 959 are exome or genome (including microarrays) which assay the entire genome sequence or structure. Finally, 79 are non-invasive prenatal tests.



Across all time periods, Concert Genetics has collected data on more than 200,000 GTUs. However, many are inactive because they've undergone a material change (e.g., adding new genes to an existing panel changes the GTU) or have been de-listed by the lab that offered them.

As a part of the Concert Genetics curation process, each GTU is categorized into a group with comparable offerings. Single-analyte GTUs are categorized with others assaying the same analyte and asking the same analytic question. Similarly, panel GTUs are categorized with others of the same indication and scope, with highly overlapping analytes and analytic questions. As such, our categories are a “generic” test type designed to facilitate side-by-side comparisons of similar tests. For more information about the categorization process, please refer to the background material at the end of this document.

## **B. NGS Tests on the Market**

Also of interest is the number of active GTUs using NGS, given the rapid proliferation of this technology. We are currently tracking 28,614 active GTUs that use NGS. Among laboratories who provide detailed information about their analytic methodologies, this represents approximately 48% of the market. Of these, 25,396 are designed to identify mutations in a single gene and 3,122 are multigene panels that look for mutations in multiple genes for a particular indication.

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### Key Takeaway:

There are almost 70,000 active genetic testing units (GTUs)  
on the market.

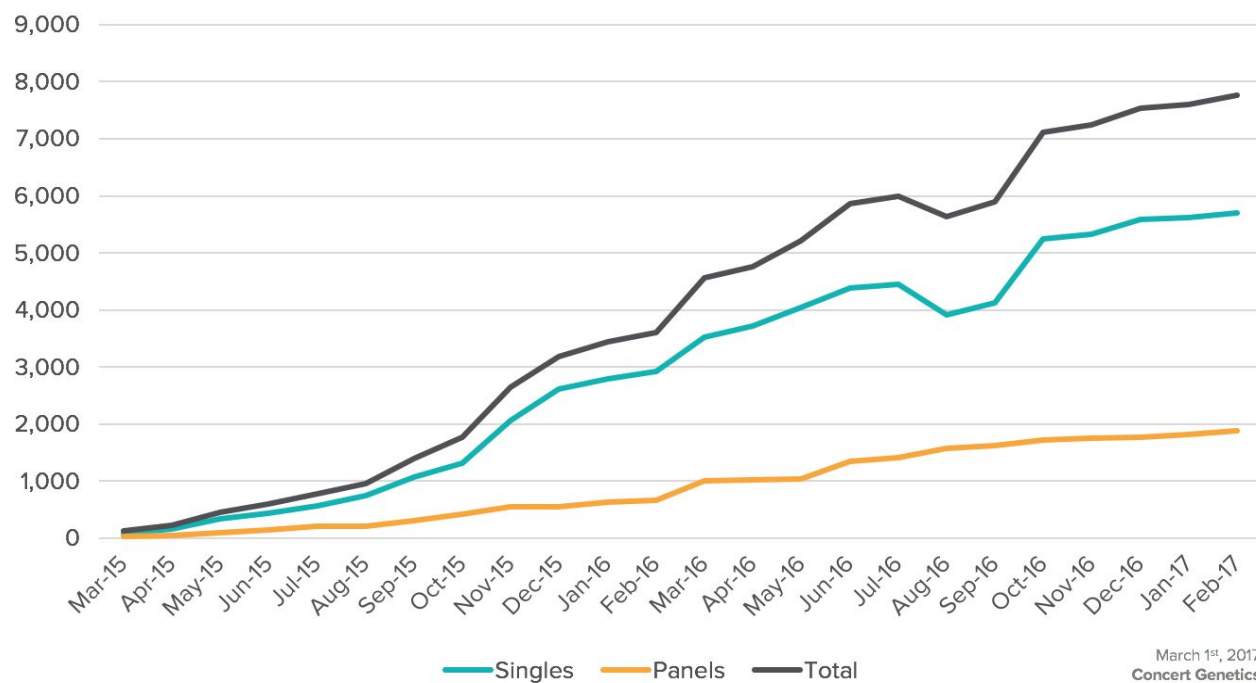
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## 2. MARKET GROWTH

### How fast is the US genetic diagnostic market growing?

Concert Genetics tracks net new GTUs added to the market on a monthly basis. In our market-wide analyses, a new GTU is defined as an orderable testing unit that is newly added to an existing catalog in our database. As we have added entire laboratories to our database, we have intentionally excluded those from this calculation, as they may have been on the market prior to our incorporation of the laboratory.

**Net New Genetic Testing Units (GTUs)  
March 1<sup>st</sup>, 2015 – March 1<sup>st</sup>, 2017**

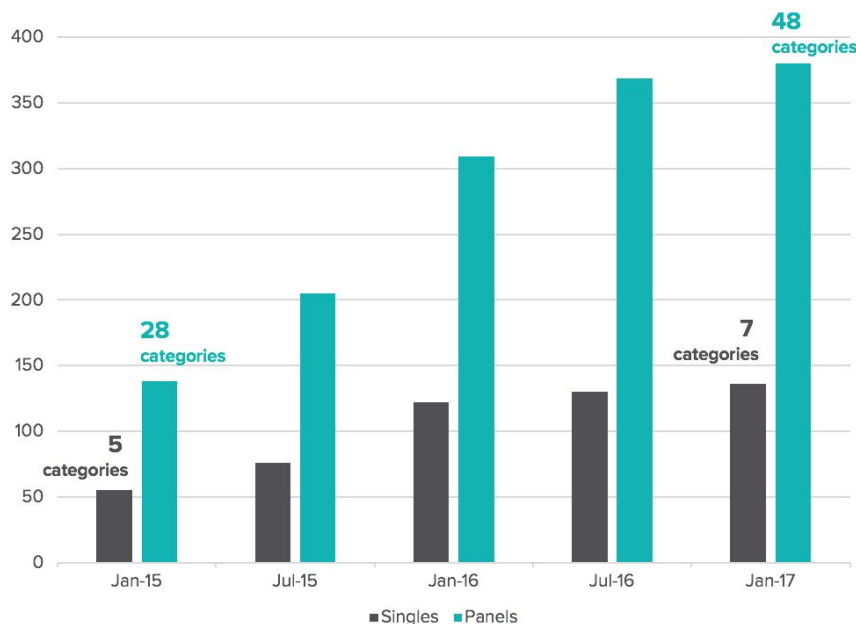


During this timeframe, an average of 10.6 new GTUs entered the market every day, which is consistent with the long-term trend we observe of approximately 10 GTUs entering the market every day. Multi-gene/multi-analyte panels are growing at approximately 14% compound annual growth rate, which is more than twice as fast as the overall market. This chart shows the number of new GTUs – single, panel, and combined – during the 24 months ending March 1st, 2017. While it's true that the raw count of new single-gene or single-analyte GTUs is larger than the number of new panel GTUs, the growth rate of panels is much higher because the total inventory of them pre-March 2015 was much smaller. The larger step changes in GTU counts in August and October 2016 are due to two separate reference labs removing and adding a large number of single-analyte GTUs.

Meanwhile, over 75% of the recent growth in the market can be attributed to NGS tests. We've seen several laboratories drastically expand their test catalogs over the last 12 months, likely owing to NGS and scalable analytic pipelines lowering the barrier to release new GTUs.

Additionally, genes are being combined into novel multi-gene panels for different indications and varying specificity in breadth of scope. For instance, both the number and categorical varieties of GTUs including the *BRAF* gene has expanded over the last two years.

### GTUs Containing *BRAF*



In January 2015, there were about 190 GTUs that assayed the *BRAF* gene. By January 2017, there were more than 500. As the number of GTUs increased, the number of categories also increased, particularly for panel tests, indicating that many of these were different or novel in the analytic questions they were designed to ask and the scope with which they ask them.

The rate of growth in genetic testing is fast by almost any measure. As a result, it's

reasonable to expect that stakeholders from across the healthcare system – clinicians, hospitals, laboratories, and health plans – are facing challenges keeping up with the rapid pace of change. Although addressing all of these challenges are outside the scope of this document, Section 4: Clinical Workflow will detail challenges and opportunities for improvement in the clinical workflow of healthcare providers.

### Key Takeaway:

The genetic diagnostic market is growing rapidly and diversifying, with much of the growth attributable to NGS. It's reasonable to expect that this rapid pace of growth presents challenges to stakeholders across the healthcare system.

## 2. CASE EXAMPLES

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### Example 1: *BRCA1* and *BRCA2* Testing

Testing for mutations in the *BRCA1* and *BRCA2* genes to identify individuals with Hereditary Breast and Ovarian Cancer Syndrome has been offered to patients for over 20 years now. For some time, testing options were limited, owing to patent protection covering the two genes. Since the AMP vs. Myriad Supreme Court decision in 2013 ruling that DNA sequences are products of nature, the market has expanded significantly and a diverse array of GTUs have been offered.

	... <i>BRCA1</i> or <i>BRCA2</i> individually?	... <i>BRCA1</i> and <i>BRCA2</i> together?	...a panel of 3 or more genes including <i>BRCA1</i> and <i>BRCA2</i> ?	... <i>BRCA1</i> and/or <i>BRCA2</i> in any form? (total)
How many GTUs analyze...	91	93	258	436
How many categories contain...	6	3	27	33
How many labs offer testing for...	22	40	49	59
How many unique gene combinations exist for...	2	1	193	196

This table demonstrates the variability in the ways that these two genes have been packaged into unique offerings: 1) As single-gene GTUs, 2) As a two-gene GTUs (historically most common), and 3) As a part of multi-gene GTUs (panels) containing other cancer risk genes. The number of multi-gene panels has grown beyond the combined total of single-gene and two-gene testing GTUs.

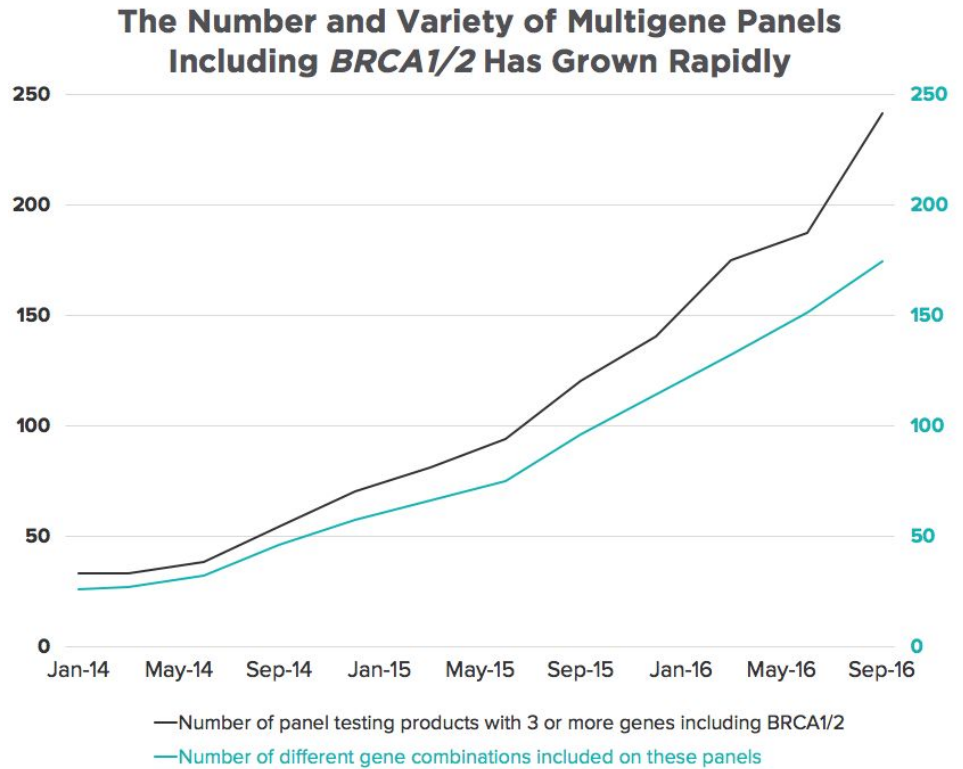
Of the 258 gene combinations we find in panels that include *BRCA1* and *BRCA2*, 193 are completely unique. Clearly, diversity of panels is increasing.



To put an even finer point on this trend, we generated this chart for a whitepaper we released in November 2016, *A Guide to BRCA Testing for Health Plans*. The data clearly show that, as labs release new panels containing 3 or more genes including *BRCA1/2*, the vast majority of these contain a completely unique combination of genes not previously available from another panel.

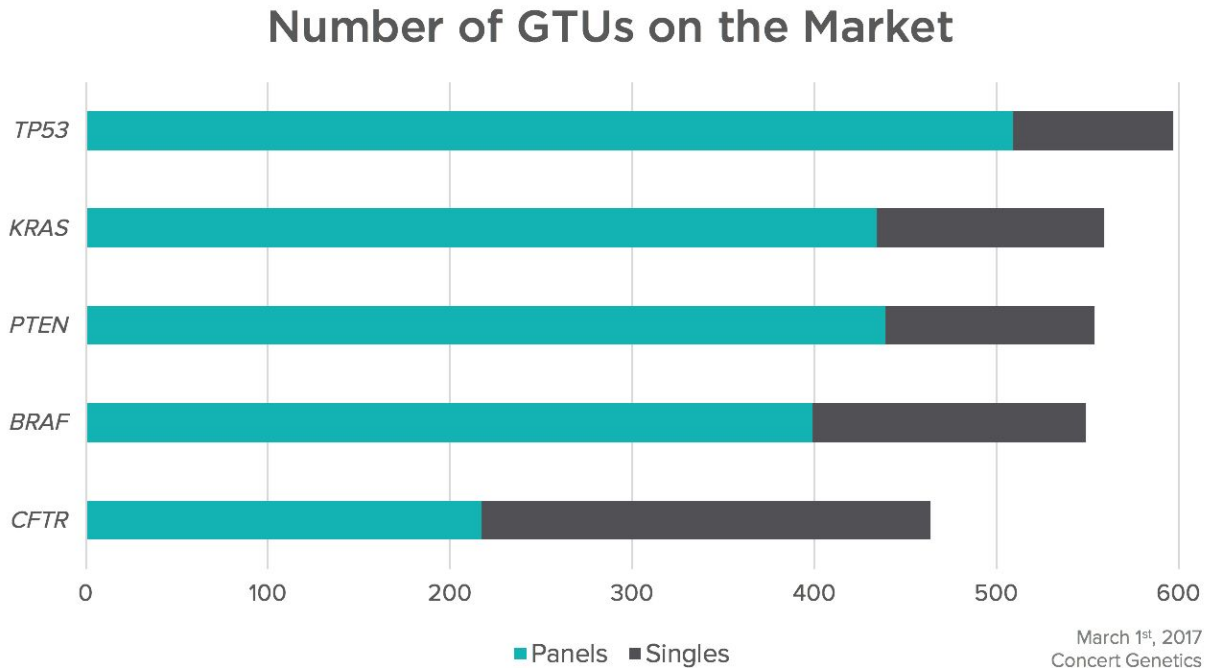
Needless to say, this diversity can be a challenge; with so many options, how can stakeholders know they've identified the right one?

Our category structure collapses these panels into 27 different clinical indications (27 categories) for which these panels are offered. In doing so, we hope to simplify the test selection process for healthcare providers, and the analytic process for researchers and health plans, by allowing for side-by-side comparisons of similar GTUs.



## Example 2: The Top 5 Genes

One gene can be studied in many ways to address a variety of clinical questions. The chart below shows the 5 most commonly assayed genes among all GTUs in the Concert Genetics database and the number of testing GTUs offered for each gene, both as a part of a panel and in isolation.



The most common gene by catalog appearance in our database is *TP53*, which appears in 597 different GTUs. Among these are over 500 panels and almost 100 single gene GTUs. Panels with *TP53* include:

- Tests for the germline hereditary cancer syndrome, Li-Fraumeni,
- Broader scope panel tests for hereditary cancer (generally), and
- Tumor profiling tests for various cancer types designed to identify somatic (tumor-specific) *TP53* mutations.

Like *TP53*, 3 of the genes (*KRAS*, *PTEN*, and *BRAF*) are included on both hereditary and somatic (tumor) tests, largely explaining their frequent appearance. *CFTR* appears frequently because of its inclusion in a wide variety of carrier testing panels.

These examples further highlight the challenging nature of the genetic testing landscape, especially for clinicians and hospital laboratories who are tasked with selecting and ordering the right test on a case-by-case basis. With 400-600 different testing GTUs for a given gene, how can healthcare providers be sure they've selected the right one? This particular issue, and other challenges related to the clinical workflow, is addressed in Section 4: *Clinical Workflow*.

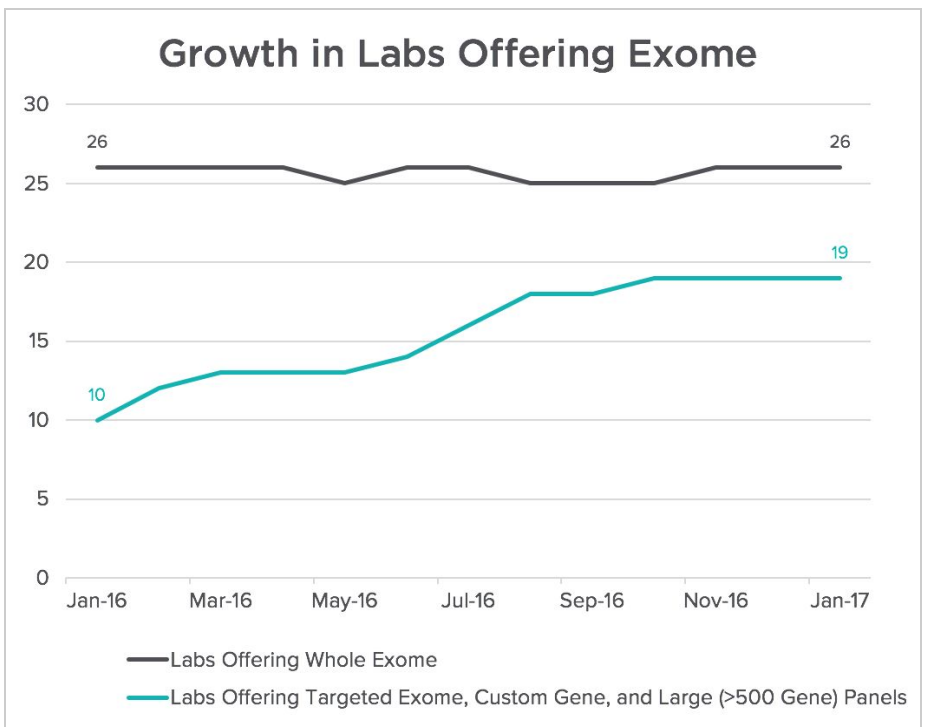
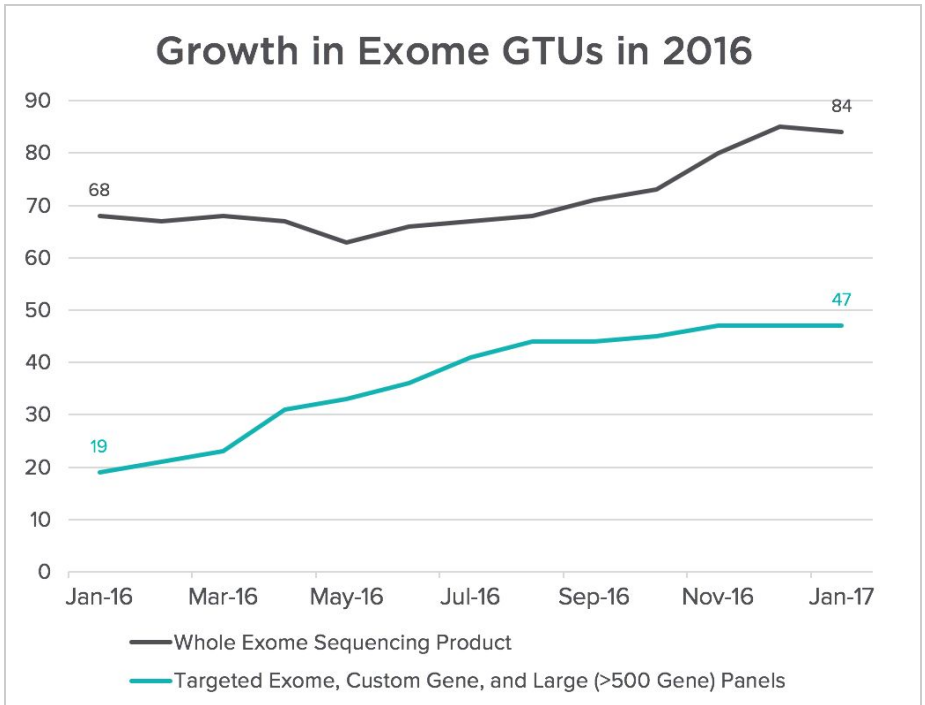
### Example 3: Exome Testing

In 2016, the number of exome GTUs on the market grew by 24%, from 68 offered in January 2016 to 84 offered in January 2017, while the number of labs offering these tests remained relatively constant.

Among laboratories that offer more than one type of exome test, variations include:

- Trio testing vs. proband only,
- The bundling of exome with microarray,
- The option to include mtDNA sequencing,
- Interpretation only services, and
- Exomes with rapid turnaround time.

Another trend observed over 2016 was steady growth in the number of targeted exome, custom gene and large (>500) gene panels. Many clinicians view these as alternatives to whole exome sequencing. In many cases, these are cheaper than a full exome, offering a cost-savings opportunity, with the option to reflex to having the remainder of the exome interpreted, if necessary. Unlike whole exomes, growth in these types of tests is largely driven by the number of laboratories entering this part of the market.

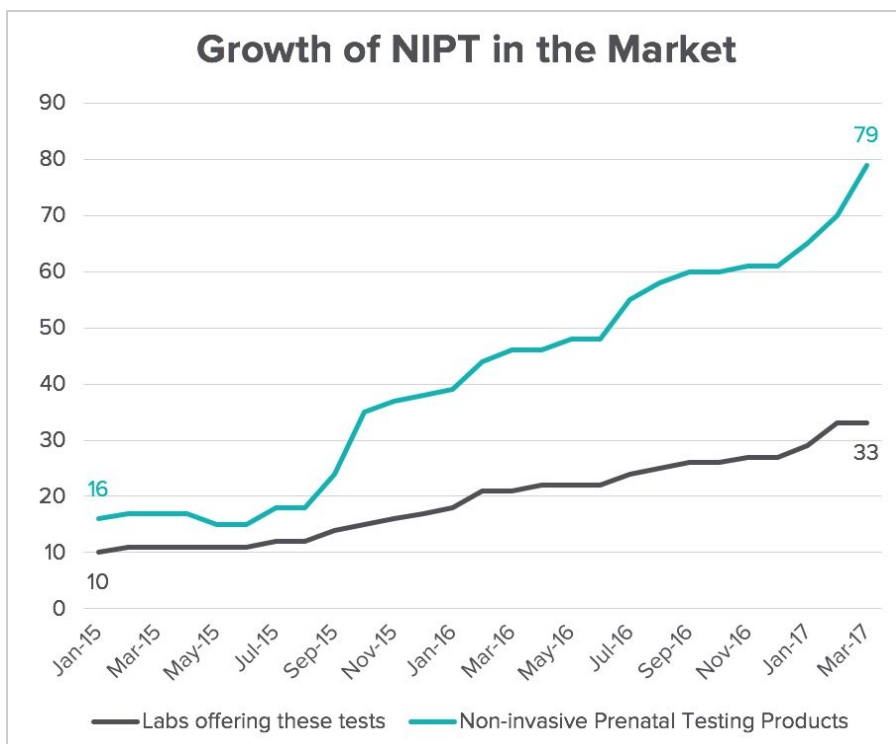


## Example 4: Non-invasive Prenatal Testing (NIPT)

Over the course of 2016, we saw significant expansion in the scope and types of NIPT tests in the market. Many of the new tests identify anomalies beyond the traditional chromosome 13, 18, 21, X and Y aneuploidies. These include identification of deletions associated with contiguous deletion syndromes, genome wide copy number variants, and, more recently, diagnosis of single gene disorders.

Recently, we split NIPT GTUs into two categories: “NIPT for Chromosome 13, 18, 21, X and Y aneuploidies” and “NIPT Expanded Panel Tests” to better distinguish new offerings in NIPT. We anticipate that this growth will continue in 2017 and expect to see many new and diverse offerings.

One other notable phenomenon in the NIPT categories is the high frequency of tests performed in one lab, but marketed by another. We refer to these tests as “sendouts” and present the overall frequency as observed in our curation process in the table below. That said, in some instances, it is unclear where a particular test is performed.



### Many NIPT Tests are Marketed by More Than One Lab

	NIPT for 13, 18, 21, X & Y	NIPT - Expanded	Total
Products	48	31	79
Labs	29	18	33
Sendouts	22	11	33

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### Key Takeaway:

Testing options for NIPT are broadening and becoming more complex, with an increasing number of laboratories expanding the scope of anomalies detected by the tests. Further complexity is added by the fact that many tests are performed in one lab, but marketed by more than one lab.

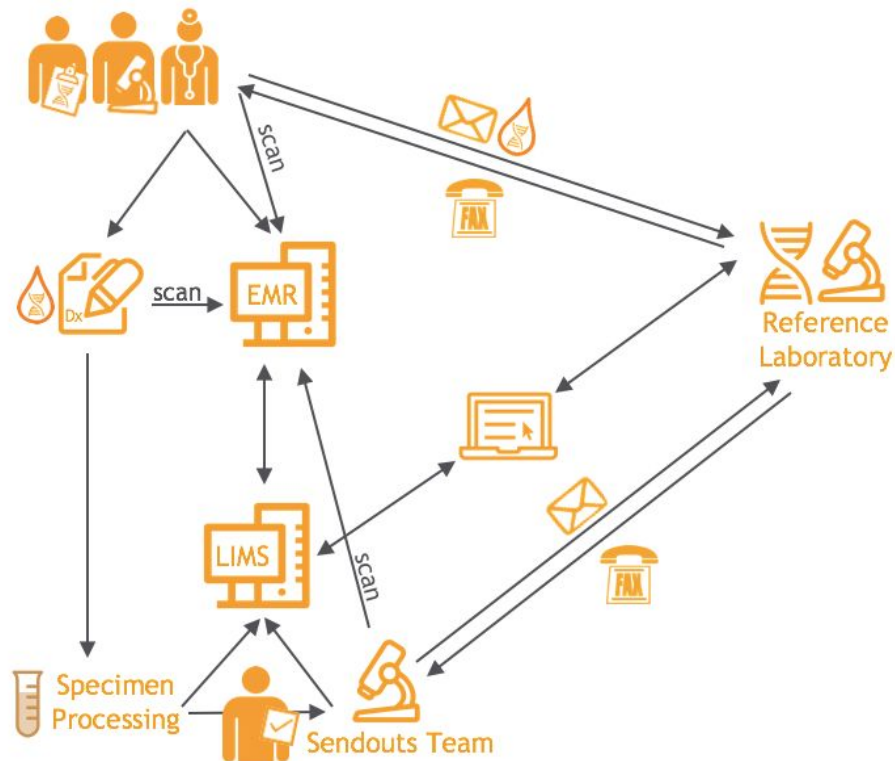
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## 4. CLINICAL WORKFLOW

### Challenges and opportunities for genetic testing in the clinical workflow.

In light of the rapid growth and complexity described in this document, it's evident why genetic testing and precision medicine don't always fit easily into the existing healthcare delivery system. Today, administrative and clinical leaders face many practical challenges in realizing the promise of precision medicine.

One key challenge is integrating genetic testing into the day-to-day operational workflow at hospitals and health systems. This challenge presents itself in the following 4 operational processes (among many others).



*Often, multiple different workflows exist within the same provider institution, further complicating the genetic testing sendout process. This graphic represents various workflows we've seen at just one institution.*

## 1. Selecting The Test And Performing Laboratory

The number of genetic testing options (GTUs) has expanded rapidly. So has the number of laboratories offering those testing options. Increasingly, hospital laboratories find themselves sending esoteric tests to dozens of different labs that specialize in various areas of genetics. This introduces complexity into many aspects of the sendout process, including test selection.

### For example:

- At many institutions, a genetic test order is initiated in the EMR using a miscellaneous test code. These orders are often sparse on information. For example, an order might identify the gene(s) to assay, but not the methodology or clinical question the test should answer.
- Knowing which laboratories offer which testing products is difficult without visiting the website of each individual lab and searching its catalog. This can be prohibitively time consuming for busy lab professionals.
- Comparing testing options between multiple labs is difficult, if not impossible, because the individual genes assayed by various testing panels often differ.
- Prices vary widely from one lab to the next, but these are inherently difficult to compare because not all laboratories publish their list prices, and because determining accurate pricing often requires a dialogue between the institution and performing laboratory.

The stakes of these issues are high. Ordering the wrong test can lead to unnecessary testing, delayed or inappropriate testing impacting patient care, and financial liability for the patient, practice, institution, or payer.

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### How the Concert Platform Helps:

The Concert Platform provides hospitals with administrative tools to lower costs and streamline institutional genetic test ordering. It allows clinicians and laboratory professionals to quickly compare and contrast almost 70,000 GTUs to enable effective, high-value choices. Within the Platform, hospitals can denote preferred labs, import their institutionally negotiated price lists to a private, institution-specific marketplace, and flag specific tests that either shouldn't be ordered or require high-level review by an institutional designee. Clinicians and laboratories are saving valuable time and money as a result of this collaborative software solution.

## 2. Placing The Order

Selecting the test is just the start. Placing the order can be equally challenging and time-consuming. Unlike ordering tests from a primary reference lab through a single, integrated portal, the process of ordering genetic sendout tests from many labs is not simple.

### For example:

- If the hospital lab isn't integrated with each of these specialized labs through a portal, it must use paper requisition forms to place orders.
- Finding the requisition form can be as time-consuming as finding the right test. Using the incorrect requisition form can delay turnaround time, and sometimes paper forms are lost altogether.
- Filling out forms by hand can be tedious and error-prone. If incorrect information is entered, patient results may be compared to the wrong reference range, a sample may need to be re-collected and/or the results may not reach the ordering provider.

This is another area where the consequences of error can be high, leading to wasted time and potentially even legal risk.

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### How the Concert Platform Helps:

Using the Platform, you may never have to find and complete another paper requisition form by hand to order a genetic test. Instead, completing the necessary information in the web-based software platform automatically populates the correct requisition form in a manner that the laboratory can effectively process. Electronic documents such as pedigrees or clinical forms can also be uploaded as support documentation for the order. Once that's done, just print the completed requisition form and ship it to the laboratory with the sample. Wasted time and the likelihood of error are both greatly reduced through this process.



### 3. Results Delivery

Failing to retrieve the results of any laboratory test that was ordered and to communicate those results to the ordering clinician (and ultimately, the patient) introduces the risk for considerable harm and even legal liability. Due to the multiple and manual ordering processes used to place genetic test orders, as well as longer-than-average turn around times, tracking results from genetic test orders can be even more difficult than other types of laboratory testing.

For example:

- Many genetic tests are not ordered frequently enough to warrant definition within the EMR or laboratory test catalog. Such orders are often entered as miscellaneous codes and are executed using a printed requisition form. Keeping an accurate record of such paper-based orders is challenging, and creates significant limitations around tracking whether orders have been sent to the reference laboratory, and more importantly, when the results are due. The results of these tests are often delivered by fax, a mechanism that is neither secure nor error-proof. If the fax transmission doesn't arrive at the right place, the test and corresponding result may be overlooked
- On the receiving end, results returned on many genetic orders are text-heavy, multi-page reports that often require special processing. Lengthy reports may need to be scanned into the EMR or uploaded as PDFs. By virtue of a different process, these results may not appear in the same location as other test results in the EMR. This makes it difficult for the ordering provider to be alerted to this information and increases the likelihood that other care providers will order duplicate testing, since it may not be immediately apparent that such testing was already performed.

Without a reliable process for retrieving results, the hospital laboratory exposes itself to unnecessary cost and risk.

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#### How the Concert Platform Helps:

The Platform keeps a record of every order placed in the system, and it delivers the results of these tests electronically. This makes it possible to have a central list of what genetic test orders were placed, which results have been returned, and which haven't. Plus, with this simplified process to manage intake of results, it's easier to create a process for getting those results into your EMR system and ensuring the results are retrieved.

#### 4. Tracking And Analysis Of Order Data

In their role as administrators, laboratory directors need to know and understand the ordering patterns at their institution so they can better manage resources for the maximum benefit of the institution and its patient population. This includes the need to understand the details around genetic test ordering. Unfortunately, this is easier said than done.

For example:

- As discussed above, due to the fact that many genetic tests are logged simply as ‘miscellaneous tests’, acquisition and review of an institution’s order history can be a daunting, manual process. Even if these records are available, it’s not easy to identify where improvements in the value equation (cost savings and quality improvements) are possible without in-depth research of dozens, if not hundreds, of laboratory websites.

Data to perform a retrospective analysis is critical for the proactive management of the lab. As the total volume of genetic testing grows, this issue will become more important.

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#### How the Concert Platform Helps:

Using the data collected through an institution’s ongoing test orders, the Platform delivers a wealth of insight through data visualization and reporting features. In addition, clinicians and scientists from Concert Genetics deliver a regular Technical Assessment, identifying new cost-savings opportunities based on an institution’s preferred laboratory relationships. You will enjoy peace of mind knowing that experts in laboratory medicine and bioinformatics regularly scour the market and assess your needs to find new ways to optimize your genetic testing send-out program.

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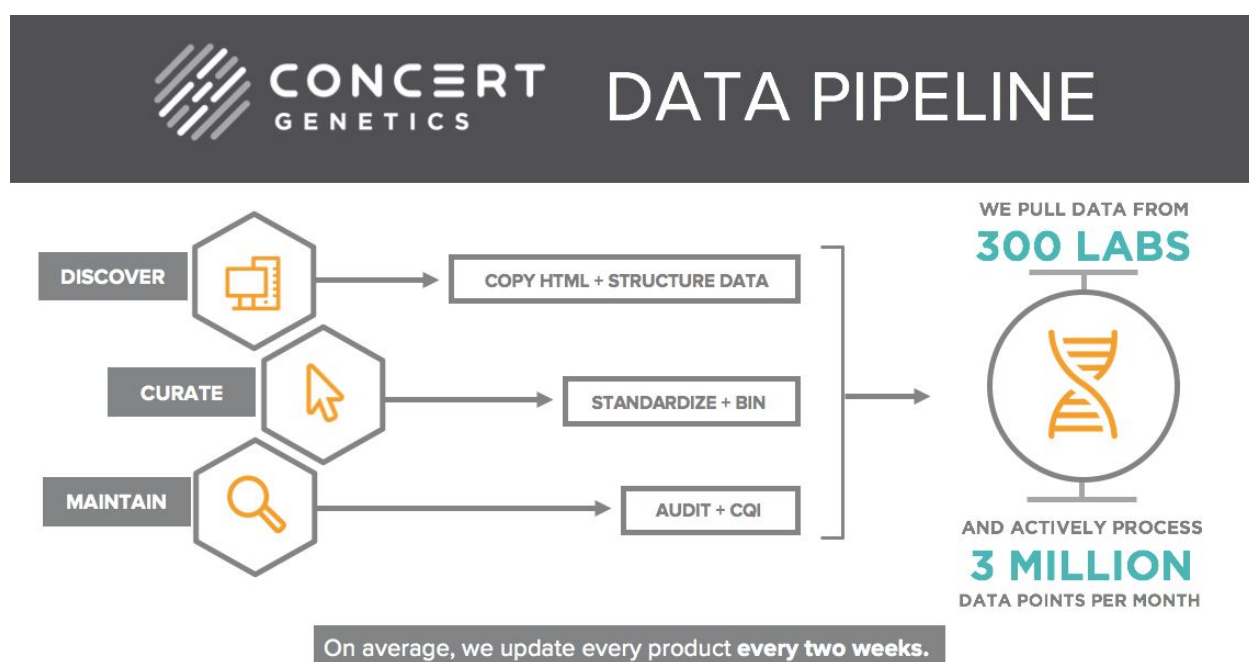
#### For more information:

If you would like to learn more about the Concert Platform or Concert Genetics, please contact Nick Tazik at (615) 861-2640 or [ntazik@concertgenetics.com](mailto:ntazik@concertgenetics.com)

## 5. DATA COLLECTION, CURATION AND ANALYTIC METHODS

### Concert Genetics And Data

Data at Concert Genetics is a first-class citizen. It drives our decision-making and the value we create for our customers and community. Due to its importance, we work to make our data as accurate, complete, and timely as possible.



### Discover

Behind the scenes, we have a team of genetic testing experts that use data science tools to collect test product information from CLIA-certified US labs, who then curate and standardize this information for use in our products.

With this system, we identify a net of approximately 10 new genetic testing products entering the market every day. As new laboratories enter the market, the Concert Genetics curation team adds these products to our searchable database, keeping it up-to-date and comprehensive for our users.

Our data collection model allows labs to avoid the process of standardizing and submitting information each time they make changes. We use the same information that laboratories use to

communicate their products to their customers – their website, marketing materials, requisition forms, etc. – along with other publicly available data sources. We make this process transparent to both users and laboratories as every piece of data is referenced back to the source of where it was collected. We also maintain active communication with the clinical and laboratory community to promote the accuracy of our test data. The major benefit of this is that within one day of a testing product being launched on a website, we can have it curated and listed in our searchable database in an appropriate, clinically relevant category.

## **Curate**

Our curated database of laboratory testing catalogs is a core component of all Concert Genetics products. When a new testing product is launched by a laboratory and enters our data curation pipeline, it is assigned a unique identifier (GTU) and we extract and associate more than 20 different data fields that describe that product. These fields facilitate comparisons of products within a category on our searchable database, streamline utilization management in our Platform, and allow for market analytics like those presented at national conferences and in various media outlets.

Once the data is separated into the appropriate fields, we standardize and curate each field according to our internal requirements. For example, manual data-entry conventions and errors can be present on laboratory websites that require standardization. These are typically minor issues like transposing two letters in a gene symbol (*IBKKAP* instead of *IKBKAP*) or dropping a letter entirely (*SERPIN1* versus *SERPINA1*). Because our customers and downstream products require a high degree of accuracy, we leverage the standards established by the clinical and scientific community to correct these errors, and where standards do not exist, we create our own. For example, we use HGNC (HUGO Gene Nomenclature Committee) to standardize genes so that the nomenclature is up to date and consistent across categories and products.

Once all the fields for each product in a lab's catalog have been appropriately structured and standardized, we then group each product into categories according to the specific analytes or genes (also known as targets), the molecular techniques it uses, and its clinical indication. After all products have been reviewed and categorized by our team, the data is sent to our searchable database and is available to all users.

## **Maintenance**

Once a lab's catalog has been curated, it is then set up to automatically check for updates to the catalog. Lab catalogs are typically monitored weekly. As new data appears, our data curation team is notified to take action. We update the catalog as appropriate through our regular pipeline and push the latest data to our searchable database.

Since no system is perfect, we also work to continually improve our processes. We regularly perform audits on every lab in the database to ensure that all relevant data is captured and every product is accurately standardized and binned. We also regularly check for inaccuracies by doing a post hoc analysis on the data in the database. Furthermore, we routinely incorporate feedback from users and laboratories, greatly strengthening our resource and making it more useful for the broader market. This enables us to perform continuous quality improvement on our data and processes.

## Analyses

All analyses performed by the team at Concert Genetics are with marketplace data at specific points in time. For this whitepaper, one time point was used for each month from January 1, 2015 to March 1, 2017 (with varying ranges depending on the specific use case).

## External Databases Used By Concert Genetics For Product Curation

- OMIM - <https://www.omim.org>
- HGNC - <https://www.genenames.org>
- Disease Ontology - <https://www.disease-ontology.org>
- Orphanet - [www.orpha.net](http://www.orpha.net)
- UNIProt - <https://www.uniprot.org>
- Ensembl - <https://www.ensembl.org>
- BioMuta - <https://hive.biochemistry.gwu.edu/tools/biomuta/index.php>

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### For more information:

If you would like to learn more about our data pipeline  
or our analyses, please contact  
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## 6. CONTACT INFORMATION

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