

The Current Landscape of Genetic Testing

Market size, market growth and the practical challenges of the clinical workflow

March 2016

EXECUTIVE SUMMARY

This report is intended to present the current landscape of 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 to build tools that bring transparency and insight to different market stakeholders.

Key points addressed in this document include:

1. Market Size

There are currently more than 60,000 genetic testing products on the US market.

2. Market Growth

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

3. Next Generation Sequencing

Much of the growth in the market is attributable to NextGen Sequencing (NGS), which accounts for more than 30% of the tests on the market and 40% of market growth.

4. Complexity and Variety

Testing options are broadening and becoming more complex, with laboratories packaging testing products in a widening variety of ways. Targeted exome products and carrier panels, specifically, are available in increasing variety, which makes distinguishing among them more difficult.

5. Clinical Workflow

Healthcare providers face mounting challenges integrating genetic testing into the clinical workflow. Utilization management tools, such as GeneConnect from Concert Genetics, 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 personalized medicine.

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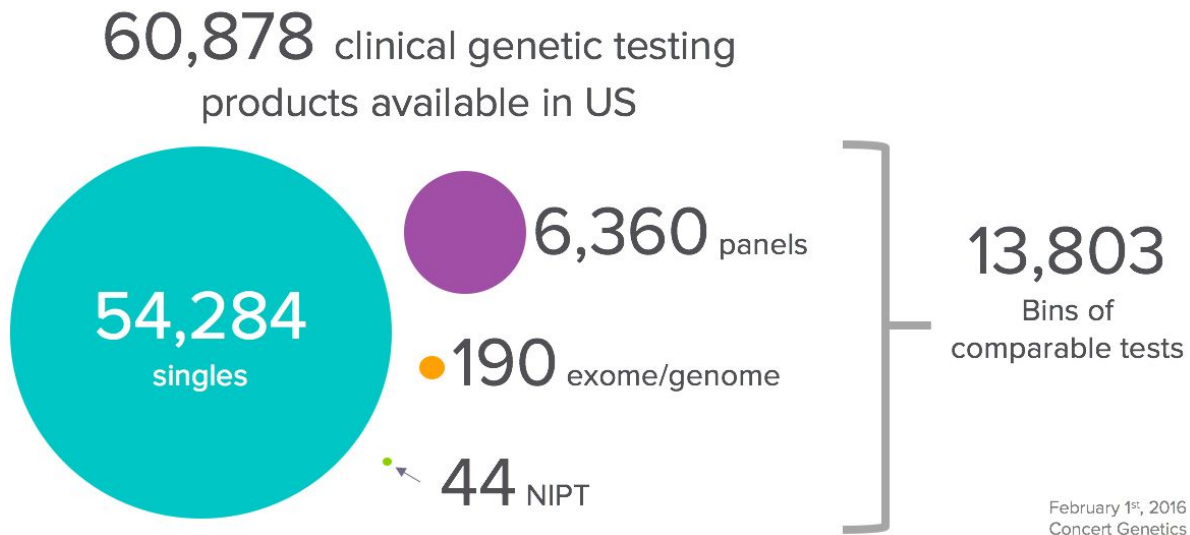
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1. MARKET SIZE

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

A. Total Testing Products on the Market

To date, Concert Genetics has collected information on 60,878 clinical testing products from more than 300 US-based, CLIA-certified labs. In our database, a testing product is defined as an orderable unit, sold by a laboratory as a single item in the laboratory’s catalog. Of these testing products, 54,284 assay a single gene or analyte. 6,360 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 190 of the testing products are exome or genome products (including microarrays) which assay the entire genome sequence or structure. Finally, 44 of the testing products are for non-invasive prenatal testing.



As a part of the Concert Genetics curation process, each testing product is binned into a group with comparable products. Single-target testing products are binned with others assaying the same target and asking the same analytic question. Similarly, panel testing products are binned with others of the same indication and scope, with highly overlapping targets and analytic questions. As such, our bins are a “generic” test type designed to facilitate side-by-side comparisons of similar products. For more information about the binning 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 NGS testing products on the market, given the rapid proliferation of this technology. We are currently tracking 18,809 NGS testing products offered in the market. This represents approximately 31% of the total products on the market, offered by 87 different CLIA-certified laboratories. Of these 18,809 NGS products, 16,712 of them are designed to identify mutations in a single gene and 2,046 are multigene panels that look for mutations in multiple genes for a particular indication.

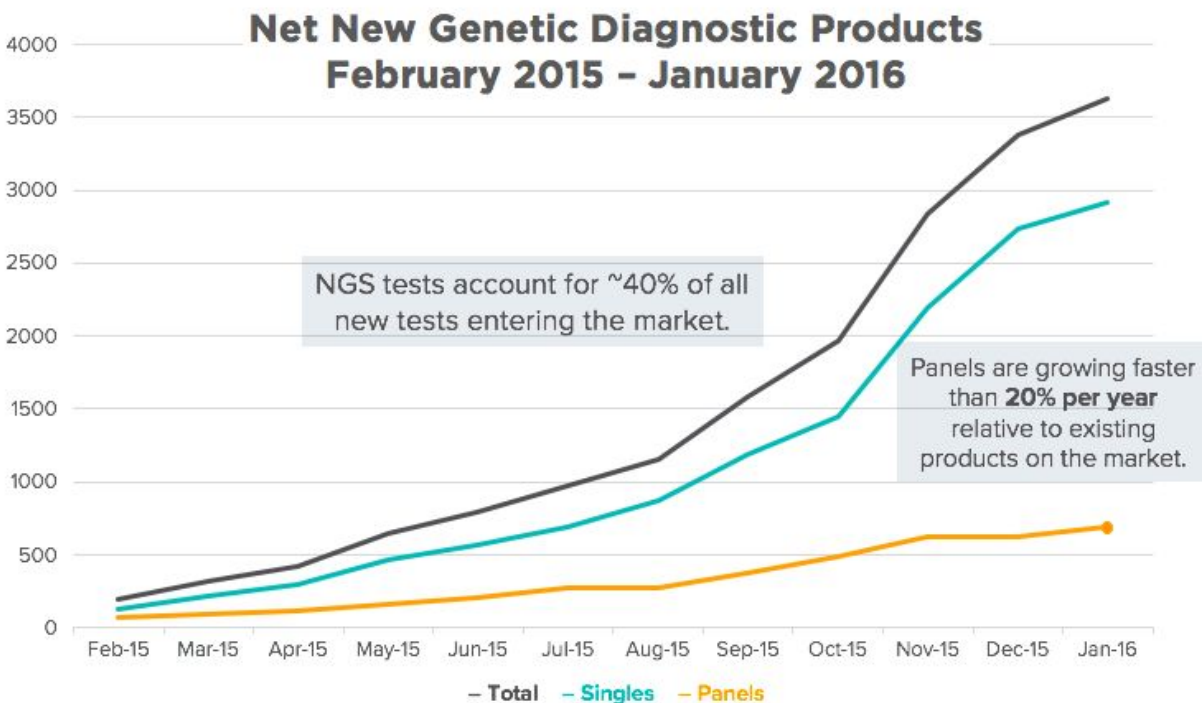
Key Takeaway:

There are more than 60,000 genetic diagnostic testing products on the market.

2. MARKET GROWTH

How fast is the US genetic diagnostic market growing?

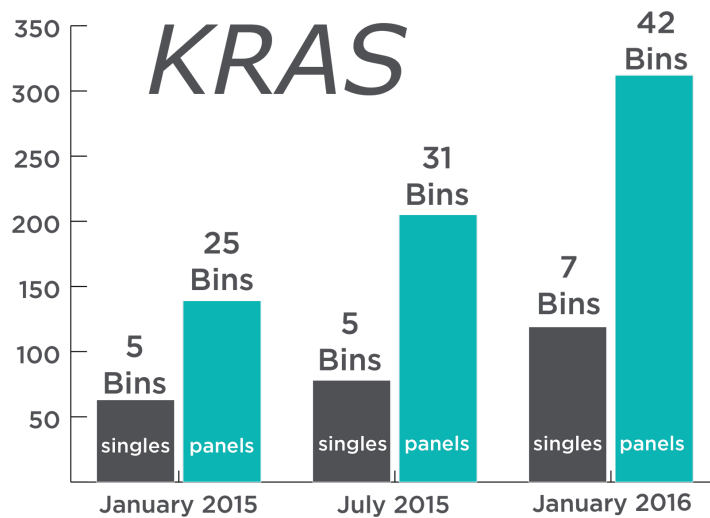
Concert Genetics tracks net new testing products added to the market on a monthly basis. In our market-wide analyses, a new testing product is defined as an orderable testing unit that is new to an existing catalog in our database. As we have added entire laboratories to our database, we have intentionally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



On average, approximately 10 new testing products enter the market every day. Multi-gene/multi-target panel tests are growing at approximately 20.8% compound annual growth rate, which is more than twice as fast as the overall market. This chart shows the number of new testing products – single, panel, and combined – during the 12 months ending February 1st, 2016. While it’s true that the raw count of new single gene testing products is larger than the number of new panel products, the growth rate of panel products is much higher because the total inventory of these products pre-2016 was much smaller.

Meanwhile, 40% of the growth in the market can be attributed to NGS tests. Further, we've seen several laboratories drastically expand their test catalogs over the last 12 months, likely owing to NGS technologies and scalable analytic pipelines lowering the barrier to developing new testing products.

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 types of testing products including the *KRAS* gene has expanded over the last year.



In January 2015, there were about 200 products for somatic (tumor) and hereditary disease (Noonan Spectrum Disorders) that assayed the *KRAS* gene. By January 2016, there were more than 400. As the number of products increased, the number of bins containing these products also increased, 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 payers – 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

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 testing products have been offered.

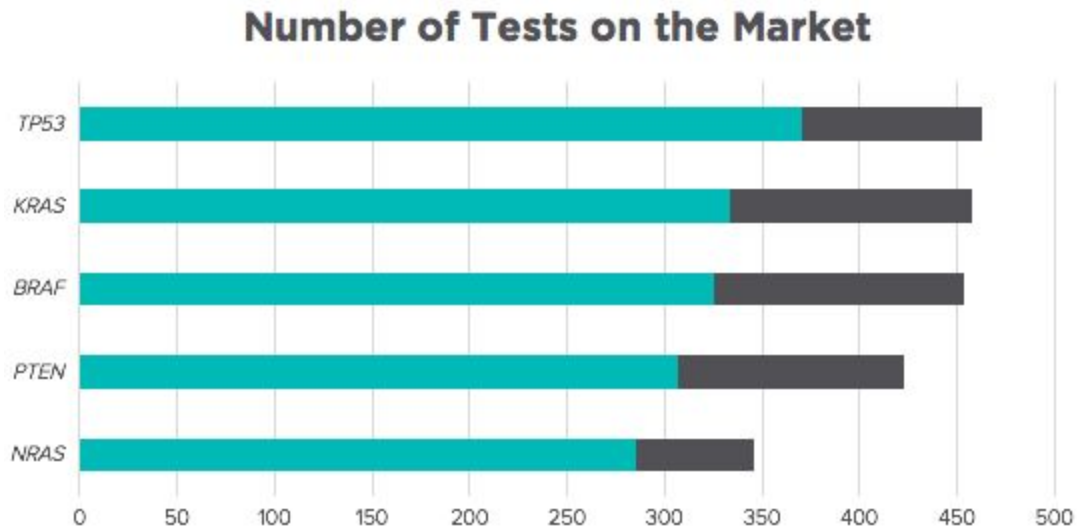
	... <i>BRCA1</i> or <i>BRCA2</i> individually?	... <i>BRCA1</i> and <i>BRCA2</i> together?	...a panel of 3 or more genes including <i>BRCA1</i> and <i>BRCA2</i> ?	... <i>BRCA1</i> and/or <i>BRCA2</i> in any form? (total)
How many products analyze...	78	85	172	335
How many bins contain...	6	3	23	31
How many labs offer testing for...	22	35	37	54
How many unique gene combinations exist for...	2	1	131	134

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

Of the 172 gene combinations we find in panels that include *BRCA1* and *BRCA2*, 131 are completely unique. This diversity can be a challenge; with so many options, how can stakeholders know they've identified the right one? Our bin structure collapses these panels into 23 different clinical indications (23 bins) for which these panels are offered. Another trend in *BRCA1/2* testing is the increasing prevalence of these genes on tumor testing panels. As of February 2016, 63 out of 335 products that included *BRCA1* and/or *BRCA2* were intended for tumor testing.

Example 2: The Top 5

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



The most common gene by catalog appearance in our database is *TP53*, which is targeted in 463 different testing products. Among these are over 350 panels and almost 100 single gene tests. 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*, the other 4 genes (*KRAS*, *BRAF*, *PTEN*, and *NRAS*), are included on both hereditary and somatic (tumor) tests, largely explaining their appearance in so many testing products.

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 300-500 different testing products 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, will be addressed in-depth later in this document.

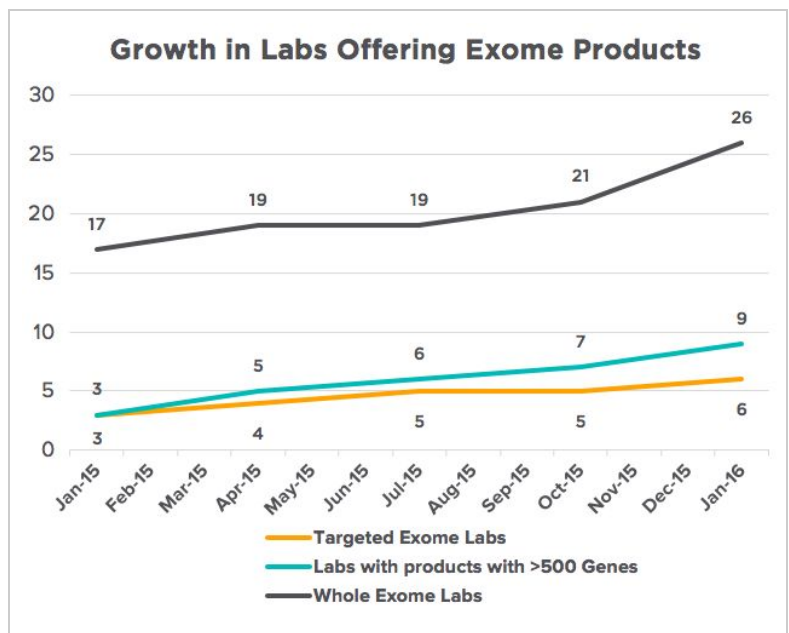
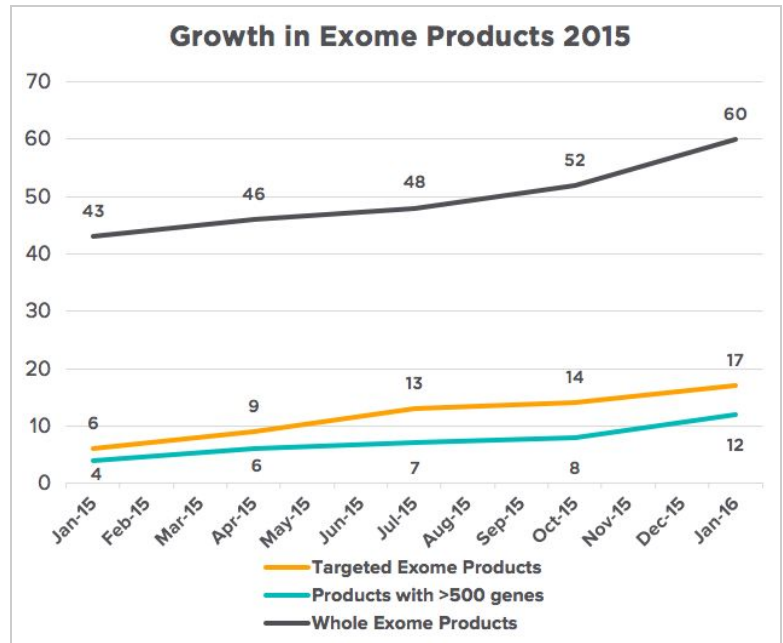
Example 3: Exome Products

In 2015, the number of exome products on the market grew by 40%, from 43 products offered in January 2015 to 60 offered in January 2016. This growth was driven, in large part, by laboratories entering the exome market, increasing the total number from 17 to 26 laboratories.

Among laboratories that offer more than one exome product, 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 2015 was steady growth in the number of targeted exome sequencing products and panel products with more than 500 genes. Many clinicians view these products as alternatives to whole exome sequencing. In many cases, these products 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. As with whole exome sequencing, growth in these types of tests is largely driven by the number of laboratories entering this part of the market.



1. Selecting The Test And Performing Laboratory

The number of genetic testing products 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 target, 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 targeted 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.

How GeneConnect Helps:

GeneConnect is a utilization management solution that provides hospitals with administrative tools to lower costs and streamline institutional genetic test ordering. GeneConnect allows clinicians and laboratory professionals to quickly compare and contrast more than 60,000 testing products to enable effective, high-value choices. Within GeneConnect, 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.

How GeneConnect Helps:

Using GeneConnect, 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.

How GeneConnect Helps:

GeneConnect 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.

How GeneConnect Helps:

Using the data collected through an institution’s ongoing test orders, GeneConnect 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.

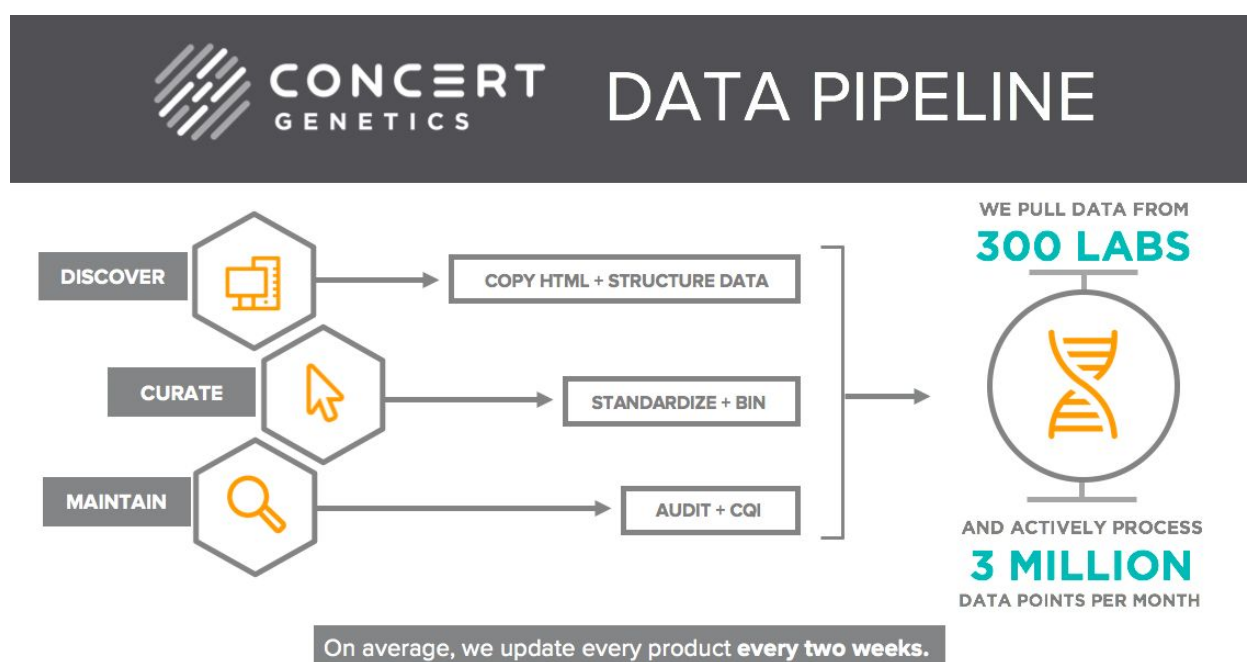
For more information:

If you would like to learn more about GeneConnect or Concert Genetics, please contact Kevin McKnight at (615) 861-2640 or kmcknight@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 bin.

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 and we extract and associate more than 20 different data fields that describe that product. These fields facilitate comparisons of products within a bin on our searchable database, streamline utilization management in our GeneConnect product, 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 bins and products.

Once all the fields for each product in a lab's catalog have been appropriately structured and standardized, we then "bin" each product according to the specific analytes or genes, the molecular techniques it uses, and its clinical indication. After all products have been reviewed and binned 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 February 1, 2016.

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
- UNIProt - <https://www.uniprot.org>
- Ensembl - <https://www.ensembl.org>
- BioMuta - <https://hive.biochemistry.gwu.edu/tools/biomuta/index.php>

For more information:

If you would like to learn more about our data pipeline
or our analyses, please contact
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