

## iCS-digital™ PSC test report

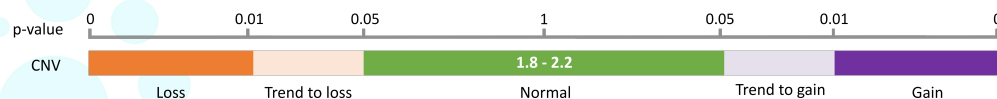
CONTACT PERSON		
Name: Francesca Stillitano	Phone: 0031 88 75 565 05	E-mail: f.stillitano@umcutrecht.nl
ORGANIZATION		
Name: UMC		
Address: Uppsalalaan 8- 3584CT Utrecht- The Netherlands		

PURCHASE ORDER (DATE)	REMAINING TEST(S)
QUOT231213-5 (19/01/2024)	13

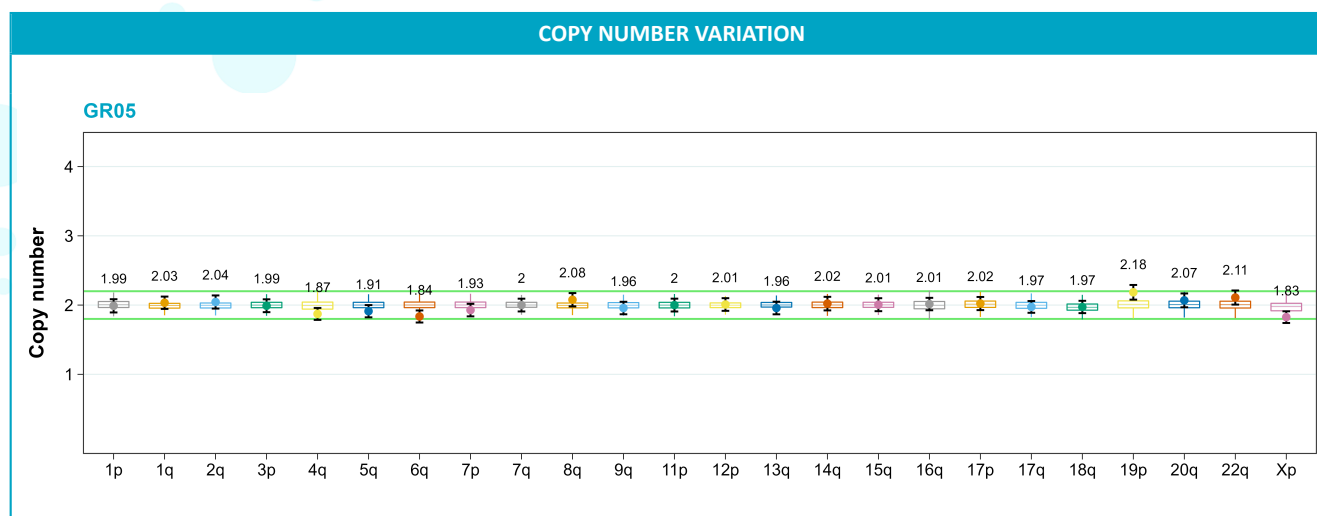
TEST DATE	CONTROL VALIDATION
May 23, 2024	Normal DNA control for the 24 probes: Passed

SUMMARY OF THE DETECTED COPY NUMBER VARIATIONS						
Sample	Cell line	Passage	dsDNA (ng/ $\mu$ L)	dsDNA quantity	CNVs	Sex *
GR05	GR05 C5	P20	25.8	Good	Not detected	F
<p>The results of this test are for research use only.</p> <p>To cite the iCS-digital™ test in your article, please select the most appropriate option from sample texts available <a href="#">here</a>.</p> <p>* If unknown, sex is deducted from the ChrX copy number; note that one ChrX can be detected in female cells that lost one ChrX, and two ChrX in male cells that gained one copy.</p>						

Copy number values:



SUMMARY OF THE DETECTED COPY NUMBER VARIATIONS																								
CHROMOSOME	1p	1q	2q	3p	4q	5q	6q	7p	7q	8q	9q	11p	12p	13q	14q	15q	16q	17p	17q	18q	19p	20q	22q	Xp
GR05																								

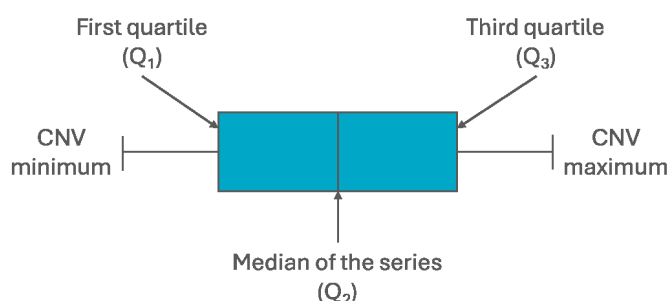


Elena HAUSER  
Platform Manager

## Appendix: iCS-digital™ interpretation method

Our technology allows for the detection of Copy Number Variations (CNVs) that is to say, DNA segments of one kilobase (kb) or larger that are present at an abnormal copy number in comparison with a reference genome. Normal copy number should be equal or close to the value of 2 at all the 24 recurrent regions that we analyze (except for the Xp position since it depends on the sex of the cell line studied: XX or XY). However, due to intrinsic variation caused by multiple factors (DNA concentration, quality, etc.), some samples will present higher copy number fluctuation than others over the 24 positions.

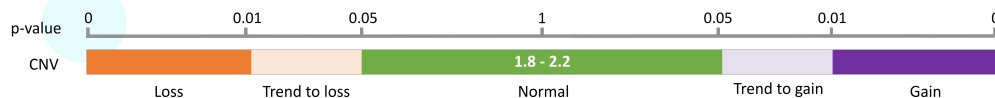
Our interpretation method takes into account the difference in CNV fluctuation observed among samples. More specifically, our statistical analysis is based on normal distribution and is adapted to the overall variability of each sample in an independent manner. P-values are then assigned to each probe and the detection of anomalies is calculated based on their specific p-values and CNVs. For each probe, a boxplot is generated based on the statistical analysis of the historical CNV values.



Visually, a non-significant value will be inside of the boxplot (indicating a similarity to a normal value) while a significant value will be outside of the boxplot (indicating a deviation from a normal value).

Green lines are displayed at 1.8 (lower limit) and 2.2 (upper limit) and represent the limit of detection of our test that is (<20% mosaicism). This means that our test can detect a minimum of 20% of abnormal cells among normal cells.

Also, a visual is shown describing the p-value and CNV thresholds detected at each position:



A sample is considered normal by default if its copy number values are strictly between 1.8 and 2.2, or if its p-values are strictly above 0.05. A trend (Trend to loss or Trend to gain), corresponds to a position detected with a p-value between 0.01 and 0.05. Trends are not anomalies but are defined as suspicion of anomalies. It could be linked to the quality of the samples, to the run, or the limit of sensitivity of the test (<20% mosaicism). In these cases, we advise to keep an eye on the samples involved and potentially re-test them few weeks/passages later.

An anomaly (CNV = Loss or Gain) is detected if a position presents a p-value strictly below 0.01.

The CNV value gives an information on the proportion of abnormal cells. For example:

- CNV = 2.2 means that 20% of the clonal population has acquired a third copy of the target region.
- CNV = 2.3 means that 30% of the clonal population has acquired a third copy of the target region.
- CNV = 3.0 means that 100% of the clonal population has acquired a third copy of the target region.
- CNV = 3.2 means that 100% of the clonal population has acquired a third copy of the target region and 20% of them has acquired a fourth copy.