Modaplex MSI Analysis Kit
Instructions for Use

For research use only. Not for use in diagnostic procedures.

Intended for use with the Modaplex System.

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LOT MSI-00001 and higher

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BIOTYPE

Contents

Product Description

The Modaplex MSI Analysis Kit is a qualitative and comprehensive PCR-based multiplex assay for the detection of microsatellite instability in human DNA derived from formalin-fixed, paraffin-embedded (FFPE) colorectal cancer (CRC) samples on the Modaplex instrument.

The assay must be used by qualified and trained personnel in a professional laboratory environment only. Results are intended solely for research use and not for diagnostic procedures.

Summary and Explanation

During replication and recombination, DNA mismatch repair (MMR) gene products identify and repair the misincorporation of bases as well as the short erroneous insertion and deletion loops [(1)]. Irreversible mutations in DNA MMR genes such as MLH1, MSH2, PMS2, and MSH6 are associated with a loss of DNA mismatch repair activity and cause genomic instability. A prominent consequence of a damaged DNA repair system is that repetitive sequences known as microsatellites become unstable and vary in length [(2)]. Thus, the presence of microsatellite instability (MSI) represents evidence that MMR is impaired [(3)].

The Modaplex MSI Analysis Kit is a fluorescent PCR-based multiplex assay intended for use with the Modaplex platform. With a combination of five quasi-monomorphic mononucleotide markers (Bat-25, Bat-26, NR-21, NR-24, Mono27) and two dinucleotide repeat markers (D5S346, D17S250), the assay supports the identification of MSI-H status in clinical research based to standardized clinical guidelines [(4)]. The resulting amplicons are separated by CE and analyzed through qualitative endpoint detection using the Moda-RA (Modaplex Result Analyzer) software version 1.4.0 and higher.

Table 1 summarizes the list of markers and internal controls.

Table 1: List of assay markers

Quasi-monomorphic mononucleotide marker	Gene loci
Bat-25	c-kit, intron 16
Bat-26	hMSH2 gene, intron 5
NR-21	*SLC7A8,* 5_UTR
NR-24	*ZNF2*, 3_UTR
Mono27	*MAP4K3*, intron 13
Dinucleotide marker	**Gene loci**
D5S346	*APC*
D17S250	*Mfd15*
Controls	**Gene loci**
HLD131	*SHH*
HLD133	*ULK4*

Principle of the Procedure

The Modaplex MSI Analysis Kit is to be used with the Modaplex platform. The microsatellite markers are amplified through fluorescent-labelled sequence-specific primers. During PCR, amplification products are injected electrokinetically and separated in an automated CE process. Electrophoresis is performed periodically every second cycle.

The microsatellite stability status is assessed using the **Moda**plex **R**esult **A**nalyzer (Moda-RA) software version 1.4.0 or higher by comparing the fragment length profiles of matching tumor and normal tissue. A deviation in length of the entire peaks or change in shape of the peaks in the tumor sample relative to the normal adjacent sample indicates MSI.

Kit format and components

The Modaplex MSI Analysis Kit contains reagents that can be used to perform 50 reactions (25 reaction pairs). It includes the following components:

MSI Primer Mix
This tube contains the oligonucleotide primers specific to seven targets (Bat-25, Bat-26, NR-21, NR-24, Mono27, D5S346, D17S250) and two internal controls (HLD131 and HLD133), as shown in Table 1.

PCR Buffer 10
This solution is optimized to promote enzyme activity for the PCR in the Modaplex MSI Analysis Kit.

Modaplex Polymerase P
The Modaplex MSI Analysis Kit contains a DNA Polymerase (2 U/µl).

Modaplex Calibrator 2
The Modaplex size standard represents a template-independent PCR control and internal length standard.

Control concept

The Modaplex MSI Analysis Kit comes with a comprehensive control concept. It consists of internal and external controls that are used to evaluate the functionality of the polymerase chain reaction and identify potential contamination. The control concept is described below:

Template-independent PCR control: Modaplex Calibrator 2
The Modaplex MSI Analysis Kit has been designed with a template-independent PCR control. In both the FAM and TYE channels, three size standards of different sizes are amplified. They represent a template-independent PCR control and internal length standard. The controls and the corresponding length are written in the table below.

Table 2: Control (Calibrator) names and lengths in FAM and TYE channel

Controls	length (bp) FAM channel
C110	110
C249	249
C306	306
Controls	**length (bp) TYE channel**
C113	113
C251	251
C309	309

Note: The Modaplex Calibrator 2 must be added to all sample, negative control and positive control wells.

Internal Controls: Human Locus Deletion/Insertion (HLD) polymorphism
These forensically accepted human deletion/insertion polymorphisms support the genetic discrimination of human individuals. The Modaplex MSI assay contains two HLD markers—HLD131 and HLD133. They are amplified within every sample and positive control well serving both as a template-dependent PCR control as well as a sample mix-up control. Additionally, they can be used to identify contamination with human sample material.

External Control 1: Negative Control (NC)
The user needs to set up a NC (no-template control) for each run to assess the potential contamination while setting up the assay. Nuclease-free water serves as a template for the NC well. In addition, the NC needs to be set up to assess the validity of the whole run. The NC is valid if no band is present at the site of the HLD marker.

Note: The user needs to set up a NC for each Modaplex run.

External Control 2: Positive Control (PC)
Human gDNA serves as PC for the MSI assay. Therefore, the PC shows a similar peak pattern as sample wells. All targets must be detectable within acceptable ranges, which confirms the proper functioning of the MSI Primer Mix. Consequently, the PC ensures that the kit performs within the stated acceptance criteria.

To confirm the proper functioning of all assay components, one PC needs to be set up for each run.

Note: The PC does not indicate instability of the microsatellite marker. Instability is a result of polymerase slippage during replication and is genetically indicated by fragment-length shifts. The primer binding site is identical for unstable and stable microsatellite markers.

Note: The user needs to set up a Positive Control for each Modaplex run.

Platform and software

Modaplex Instrument
The Modaplex MSI Analysis Kit is designed to be used with the Modaplex instrument (software version 1.4.0. or higher). This platform is a fully automated bench-top system for molecular diagnostic applications. It combines qPCR with capillary electrophoresis (CE) in an automated process and enables the detection, differentiation, and quantification of up to 50 DNA and RNA targets in a single well and run. Therefore, it enables the individual combination of tests for fragment analysis, mutational analysis, gene expression, copy-number variation, etc.

Biotype Moda-RA Software
It is strongly recommended that the Modaplex MSI Analysis Kit is analysed using Biotype's Moda-RA (**Moda**plex **R**esult **A**nalyzer) software. The software contains all the information required for the analysis of the stability of each microsatellite. No special updates, dongles, or unlocking procedures are required to start the interpretation of the results. Please refer to 'Interpretation of the Results' on Pages 15–32 for detailed information on the use of the Moda-RA software for microsatellite variation analysis.

Materials Provided

Kit contents

Table 3 summarizes the contents of the Modaplex MSI Analysis Kit and indicates the required storage conditions.

Table 3: Content of the Modaplex MSI Analysis Kit

Component	Vials	Vol./Vial (µL)	Cap Color	Storage
MSI Primer Mix	1	125	Red	−15 °C to −25 °C
PCR Buffer 10	1	625	Black	−15 °C to −25 °C
Modaplex Polymerase P	1	25	Orange	−15 °C to −25 °C
MSI Positive Control	1	65	White	−15 °C to −25 °C
Nuclease-Free Water	1	1,500	Light blue	−15 °C to −25 °C
Modaplex Calibrator 2	2	25	Yellow	−15 °C to −25 °C

Note: Non-Hazard Statement (NHS) and Safety Data Sheet (SDS) are available upon request from Biotype GmbH.

Package Inserts

The Modaplex MSI Analysis Kit is delivered with one packaging insert with two Modaplex Barcodes. Each kit must be used with the packaging inserts supplied therein. This guarantees that the test is set up according to the correct Modaplex assay definitions used for MSI analysis. The packaging insert is described in the following subsections.

Modaplex Barcodes

Two barcodes are provided for the detection and quality assessment of sample and control wells. Prior to the first use of a new lot of the MSI Analysis Kit, both barcodes must be scanned. On scanning the barcodes, MSI-related assay specifications such as assay ID, expiration date, lot number, list of targets, and internal controls are automatically transferred to the Modaplex instrument and, subsequently, to the Moda-RA software.

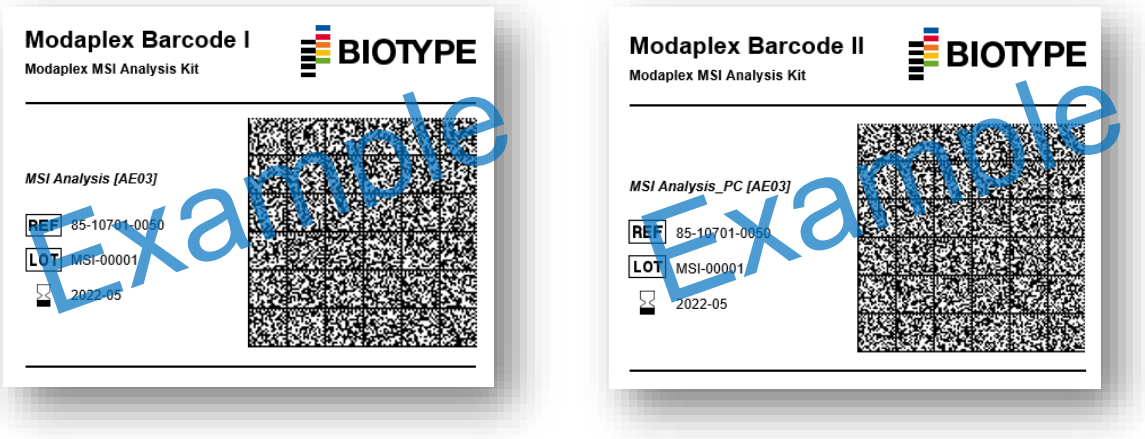


Figure 1: Example: Modaplex Barcode I and Barcode II

Modaplex Barcode I contains all MSI kit-related information required for the fragment analysis of MSI.

Modaplex Barcode II contains all information required for the assessment of the PC validity. The assessment of the PC validity differs from the detection of MSI in sample wells. Microsatellite markers and internal control targets must be called on constant fragment length positions in the PC well. In contrast, the sample well algorithm must allow for a flexible assignment of microsatellites, which is the consequence of microsatellite allele variability across ethnicities and individuals. In addition, a further size shift is introduced in case of MSI.

To ensure full traceability of kit lot numbers and expiration dates, both assay-specific Modaplex barcodes need to be scanned prior to the first use of a Modaplex MSI Analysis Kit. With each new lot of the assay, the newly provided barcodes need to be scanned, which results in new assay definitions on the Modaplex instrument, including the new lot numbers and the expiration dates.

Note: In terms of traceability, the assay specifications are present in the Moda-RA report once the barcodes have been scanned and a Modaplex run has been performed with the new MSI Analysis Kit.

Note: The Moda-RA configuration identifier is shown in square brackets behind the assay name. This unique code enables the analysis of the results in the Moda-RA.

Modaplex MSI Analysis Instructions For Use (IFU)

The Modaplex MSI Analysis Kit IFU is not provided in the Modaplex MSI Analysis Kit.

For successful download, please refer to the following instructions.

1. **Open** Biotype GmbH´s webpage using the link given on the Modaplex MSI Analysis Kit box label.

2. **Click** on the respective IFU link in the IFU download section.

Note: If the laboratory environment does not provide access to the internet, please contact Biotype GmbH´s support at support@biotype.de and request the dedicated IFU.

Materials Required (Not Included in the Kit)

In addition to the kit content, the following reagents, consumables, and equipment are required but not provided with the Modaplex MSI Analysis Kit.

Reagents and Consumables

- 10X Capillary Protection Buffer (Biotype)
- DNA extraction kit and consumables (QIAGEN Cat# 56404, Cat# 19101, Cat# 19093)
- DNA quantification kit and consumables (Thermo Fisher Cat# Q32850 or Q32851)
- Sterile Filtered nuclease-free pipette tips (various suppliers)
- Sterile microcentrifuge tubes (various suppliers)
- TE Buffer, pH 8.0 (Thermo Fisher Cat#: 10006044)
- PCR Microplates 96 (Life Technologies GmbH)
- Mineral Oil (SIGMA)
- Aluminium Sealing Film (Thermo Fisher)
- Modaplex CE 48 (Cartridge) (Biotype)
- Modaplex Buffer (Biotype)
- Modaplex Decon (Biotype)
- Modaplex Wash (Biotype)
- POP-7/ Modaplex CE Gel (Thermo Fisher)
- Modaplex CE Plates (Biotype)

Instruments and Software

- Modaplex System (Biotype)
- Moda-RA Analysis Software (Biotype)

Equipment

- Micropipettes (various suppliers)
- Bench-top centrifuge with rotor for 2ml reaction tubes (various suppliers)
- Bench-top centrifuge with plate adaptor (various suppliers)
- Bench-top vortex (various suppliers)

Warnings and Precautions

For research use only. Not for diagnostic use. Intended for use with the Modaplex instrument.

Safety Information

General Safety Information

When working with chemicals, always wear a suitable lab coat, disposable gloves, and protective goggles.

For more information about the Modaplex MSI Analysis Kit components, please consult the corresponding non-hazard statements (NHS) and safety data sheets (SDS), which are available upon request. For the safety information of the components not provided with the kit, please contact the respective supplier.

Modaplex Safety Information

Due to the high voltage required for the CE separation, failure to fill all wells is a general safety threat that may cause damage to the Modaplex instrument.

General Precautions

The user should always pay close attention to the following:

- Follow good laboratory practice guidelines.
- Only skilled laboratory technicians who are properly trained to perform reactions using PCR technology should be allowed to use this product.
- Clean and disinfect all surfaces according to the laboratory's standard operating procedure (SOP) guidelines.
- Use DNase-, RNase-, and DNA-free pipette tips with filters. Ensure that the pipettes have been calibrated according to the manufacturer's instructions.
- Change pipette tips after each pipetting step to avoid sample mixing and cross-contamination.
- Do not reuse disposables.
- Open and close the reagent containers carefully.
- Follow the instructions for reagent storage and handling.
- Ensure that the reagents are not exposed to light during storage.
- Do not use reagents beyond their expiration dates.
- Any wells in the PCR plate that are not being used for testing samples must be filled with 25 µL of 1x Capillary Protection Buffer, included in the 10X Capillary Protection Buffer Kit, and overlaid with mineral oil.
- Do not substitute the reagents with equal reagents from other manufacturers.
- Do not substitute the equipment listed in this document.
- Follow the instructions in the Modaplex System User Manual for the proper operation of the Modaplex System.
- Non-Hazard Statements (NHS) and Safety Data Sheets (SDS) are available upon request from Biotype GmbH.

Note: Use extreme caution to prevent the contamination of the PCRs with control material. We recommend using separate, dedicated pipettes for setting up the reaction mixes and adding the DNA template. To avoid potential (cross-) contamination issues, separate the different procedure steps into at least two distinct working areas—one clean area for the preparation of the PCR master mixes and a second area for the addition of the DNA template samples to the PCR reactions and the operation of the Modaplex instrument.

Note: The reagents are validated for manual set-up. Using an automated method may reduce the number of possible reactions due to the reagent required to fill 'dead volumes' on these instruments.

Note: All reagents in the Modaplex MSI Analysis Kit are formulated specifically for use with the stated test. All the reagents supplied in the kit are intended to be used solely with the other reagents in the same Modaplex MSI Analysis Kit. The reagents in the kit must not be substituted if optimal performance is to be maintained.

Note: Use only the DNA polymerase (Modaplex Polymerase P) provided in the kit. Do not substitute with a DNA polymerase from other kits of the same or any other type DNA polymerases from another supplier.

Reagent Storage and Handling

The Modaplex MSI Analysis Kit is shipped on dry ice. Upon receipt, the assay should immediately be stored at −15 °C to −25 °C in a constant-temperature freezer. The fluorescent-labelled molecules must be protected from light to avoid photobleaching. If stored under the recommended storage conditions in the original packaging, the kit will remain stable until the expiration date stated on the label.

- Repeated thawing and freezing (>5 cycles) should be avoided.
- Do not use expired or incorrectly stored components.
- All kit components are optimally diluted and no further treatment is necessary.

Note: Upon receipt, please check the Modaplex MSI Analysis Kit immediately and contact Biotype GmbH's technical support if:

- A component is not properly frozen.
- The kit labels are damaged.
- The outside boxes have been opened.
- The reagents are not present.
- The packaging inserts (Modaplex Barcodes) are missing.

Procedure

The Modaplex MSI Analysis Kit has been verified with human gDNA and DNA samples extracted from formalin-fixed, paraffin-embedded (FFPE) colorectal cancer (CRC) tissue. In addition, DNA samples extracted from formalin-fixed paraffin-embedded (FFPE) endometrial cancer tissue have been tested for use with the Modaplex MSI Analysis Kit.

DNA purification

It is recommended that DNA be purified with the QIAamp DNA FFPE Tissue Kit (QIAGEN, Cat#: 56404), Deparaffinization Solution (Qiagen Cat# 19093) and RNase A (100 mg/mL) (Qiagen Cat# 19101). Additional step is the Proteinase K digestion overnight using 3 FFPE-sections up to 10 µm (surface up to 250 mm^2). DNA purification should be carried out from macro-dissected FFPE tissue according to the supplier's instructions.

Note: The Modaplex MSI Analysis Kit is designed for use with short PCR products. However, the assay will not work with heavily fragmented DNA.

Note: After the DNA isolation procedure and prior to storage, the DNA concentration must be promptly measured.

DNA quantification

Quantification of the DNA should be carried out by fluorometric quantitation using the Qubit™ 3.0 Fluorometer. Both the Qubit™ dsDNA HS Assay (Cat#Q32851) and the Qubit™ ds DNA BR Assay (Cat#Q32850) can be used to measure the DNA concentration after isolation. The DNA concentration of the sample should be 2 ng/µl to perform the Modaplex MSI Analysis Kit at the optimal input of 10 ng.

It is not advised to use less than 2 ng/µl. An insufficient amount of DNA could lead to low PCR yields and the peak heights may fall below the target-specific detection limits. Excessive amounts of DNA >20 ng may lead to peak heights with a disturbed migration size resulting in incorrect assignments of calibrators, control amplicons, and MSI targets.

Note: If sample material other than the indicated CRC or endometria cancer FFPE tissue is used with the Modaplex MSI Analysis Kit, a verification of the input DNA amount is recommended.

Note: For sample dilution we recommend the use of 1x TE (Tris-EDTA)- Buffer, pH value 8.0 and a sample volume > 1.5 µL.

Protocol: Preparing the Modaplex run for MSI Analysis

This protocol is intended for the preparation of the Modaplex instrument, prior to the set-up of the Modaplex MSI Analysis Kit run.

1. Determine the number of PCR reactions.

Before setting up the Modaplex instrument run, the number of PCR reactions should be determined. The following controls should be included in the calculation:

- One negative control (NC)
- One positive control (PC)

2. Determine which wells are to be filled with the 1x Capillary Protection Buffer.

This number is based on the number of capillaries on the cartridge, minus the total number of PCR reactions to be performed.

3. Scan both MSI assay definitions into the Modaplex instrument.

Scan the two Modaplex barcodes provided with the Modaplex MSI Analysis Kit. The assay definitions are automatically added to the Modaplex System. See the Modaplex System User Manual for further instructions.

Note: The Modaplex barcodes need to be scanned every time a new lot of the Modaplex MSI Analysis Kit is used.

4. Confirm the Modaplex settings for the MSI Modaplex run.

Before setting up the Modaplex MSI Analysis Kit, the following conditions regarding the consumables should be satisfied for the planned Modaplex run:

- Sufficient number of remaining runs in the Modaplex cartridge
- Adequate quantity of the consumables

Note: To replace the Modaplex System cartridge or the consumables, please refer to the Modaplex System User Manual for further instructions.

5. Create a run definition and a plate map on the Modaplex instrument.

For overall evaluation and data assignment**,** the Moda-RA software requires the following form of **sample-naming:**

- Tumor tissue (= sample): *sample name_s*
- Normal adjacent tissue (= control): *sample name_c*
- Positive control: *assay name_PC*
- Negative control: *assay name_NC*

Note: It is required to use the same name for both the tumor tissue and normal adjacent tissue from the same patient before the underscore. This is a prerequisite for the Moda-RA Software to be able to align the electropherograms of the two samples automatically.

Note: The sample name can be any unique name, number, or code that can identify a sample. Sample names must be unique for each pair. If there are duplicates on one plate, the naming must differ between them. Avoid special symbols like double quotes (“), brackets (< or >), ampersands (&), etc.

Note: Remove all quality-control ticks in the plate set-up window as no absolute quantification is taking place.

Figure 2: Plate set-up window of the Modaplex software. Left: Quality control fields with ticks; Right: Quality control fields without ticks.

Protocol: Setting up the MSI Analysis Modaplex run

This protocol is for the preparation of reagents in the Modaplex MSI Analysis Kit and the PCR plate for the Modaplex run.

1. **Remove and thaw** the following components from the Modaplex MSI Analysis Kit:
   - PCR Buffer 10 (black cap)
   - MSI Primer Mix (red cap)
   - Nuclease-Free Water (light-blue cap)
   - MSI Positive Control (white cap)
   - Modaplex Polymerase P (orange cap)
   - Modaplex Calibrator 2 (yellow cap)

   Note: The Modaplex Polymerase P is temperature-sensitive. Always keep the enzyme at −15 °C to −25 °C.

2. **Remove and thaw** the 10X Capillary Protection Buffer (purple cap)

3. **Homogenize** the thawed reagents by inverting the tubes, pipetting, or gently vortexing. After this, briefly centrifuge the reagents.

4. **Preparing the MSI master mix.**

   Prepare the PCR reagent master mix (MMx) in an appropriately sized microcentrifuge tube for the total number of samples to be tested in a dedicated clean area. Use Table 4 to determine the volume of each reagent.

   Table 4: MSI master mix (MMx): The volumes of the reagents needed for the master mix.

Component	Volume of Reagents Calculated According to the # of tests					
	# 1	# 2	# 3	# 4	# 5	# 10
PCR Buffer 10	12.5 µL	25.0 µL	37.5 µL	50.0 µL	62.5 µL	125.0 µL
Nuclease-Free Water	3.5 µL	7.0 µL	10.5 µL	14.0 µL	17.5 µL	35.0 µL
MSI Primer Mix	2.5 µL	5.0 µL	7.5 µL	10.0 µL	12.5 µL	25.0 µL
Modaplex Calibrator 2	1.0 µL	2.0 µL	3.0 µL	4.0 µL	5.0 µL	10.0 µL
Modaplex Polymerase P (2.0 U/µL)	0.5 µL	1.0 µL	1.5 µL	2.0 µL	2.5 µL	5.0 µL
Total Volume of Master Mix (MMx)	**20 µL**	**40 µL**	**60 µL**	**80 µL**	**100 µL**	**200 µL**

   Note: As a rule of thumb, if you are testing fewer than 10 samples, use enough master mix for one extra sample. If you are testing 10 or more samples, use an excess reagent master mix volume of +10%.

5. **Mix gently** by inverting the tube or by pipetting. Spin down briefly in a bench-top microcentrifuge.

6. **Aliquot 20 µL** of the MSI master mix to the designated wells in the PCR plate.

7. **Add 5 µL** each of the following:
   - Extracted (prediluted) DNA (template, optimum 10 ng) to the corresponding sample well(s)
   - Nuclease-Free Water to the negative control well
   - MSI Positive Control to the positive control well

   Note: Thus, the total volume of the PCR reaction is 25 µL. Refer to Figure 3 for an example of the sample plate layout.

8. **Add 25 µL** of **1x Capillary Protection Buffer** to the remaining empty wells which are not being used for a sample well, NC or PC.
   - Prepare a 1:10 dilution of the 10x Capillary Protection Buffer in water.

- Add 25 µL of the 1x Capillary Protection Buffer to each of the empty wells. Please refer to the plate map set-up in the Modaplex System IFU for further explanation.

Due to the high voltage required for the CE separation, failure to fill all wells is a general safety threat and may damage the Modaplex instrument.

	1	2	3	4	5	6	7	8	9	10	11	12
A	Sample 01 Tumor MMx	Sample 01 Native MMx	Sample 09 Tumor MMx	Sample 09 Native MMx	Sample 17 Tumor MMx	Sample 17 Native MMx						
B	Sample 02 Tumor MMx	Sample 02 Native MMx	Sample 10 Tumor MMx	Sample 10 Native MMx	Sample 18 Tumor MMx	Sample 18 Native MMx						
C	Sample 03 Tumor MMx	Sample 03 Native MMx	Sample 11 Tumor MMx	Sample 11 Native MMx	Sample 19 Tumor MMx	Sample 19 Native MMx						
D	Sample 04 Tumor MMx	Sample 04 Native MMx	Sample 12 Tumor MMx	Sample 12 Native MMx	Sample 20 Tumor MMx	Sample 20 Native MMx						
E	Sample 05 Tumor MMx	Sample 05 Native MMx	Sample 13 Tumor MMx	Sample 13 Native MMx	Sample 21 Tumor MMx	Sample 21 Native MMx						
F	Sample 06 Tumor MMx	Sample 06 Native MMx	Sample 14 Tumor MMx	Sample 14 Native MMx	MSI_PC MMx	MSI_NC MMx						
G	Sample 07 Tumor MMx	Sample 07 Native MMx	Sample 15 Tumor MMx	Sample 15 Native MMx	Empty 1x IB	Empty 1x IB						
H	Sample 08 Tumor MMx	Sample 08 Native MMx	Sample 16 Tumor MMx	Sample 16 Native MMx	Empty 1x IB	Empty 1x IB						

Figure 3: Example of a sample plate layout for 21 samples (tumor: tumoral tissue; native: normal adjacent tissue).

9. **Seal** the PCR plate with aluminium sealing film. Gently vortex and spin the PCR plate in a table-top centrifuge.

10. **Remove** the seal and **overlay** all 48 wells on the PCR plate with **one drop of mineral oil**. Ensure that each reaction is fully covered by oil.

11. **Seal** the PCR plate again with aluminium sealing film. Spin the PCR plate and CE plate in a table-top centrifuge.

The plate cover seals must be **removed** from the PCR plate and the CE plate before they are placed on the Modaplex instrument.

12. **Run the PCR plate** in the Modaplex instrument.

13. **End of Run**

At the end of the run, **seal** the PCR and CE plates with aluminium sealing film before disposing of the plates. Decontaminate the hold-down plate.

Note: Refer to the Modaplex System IFU for further instructions

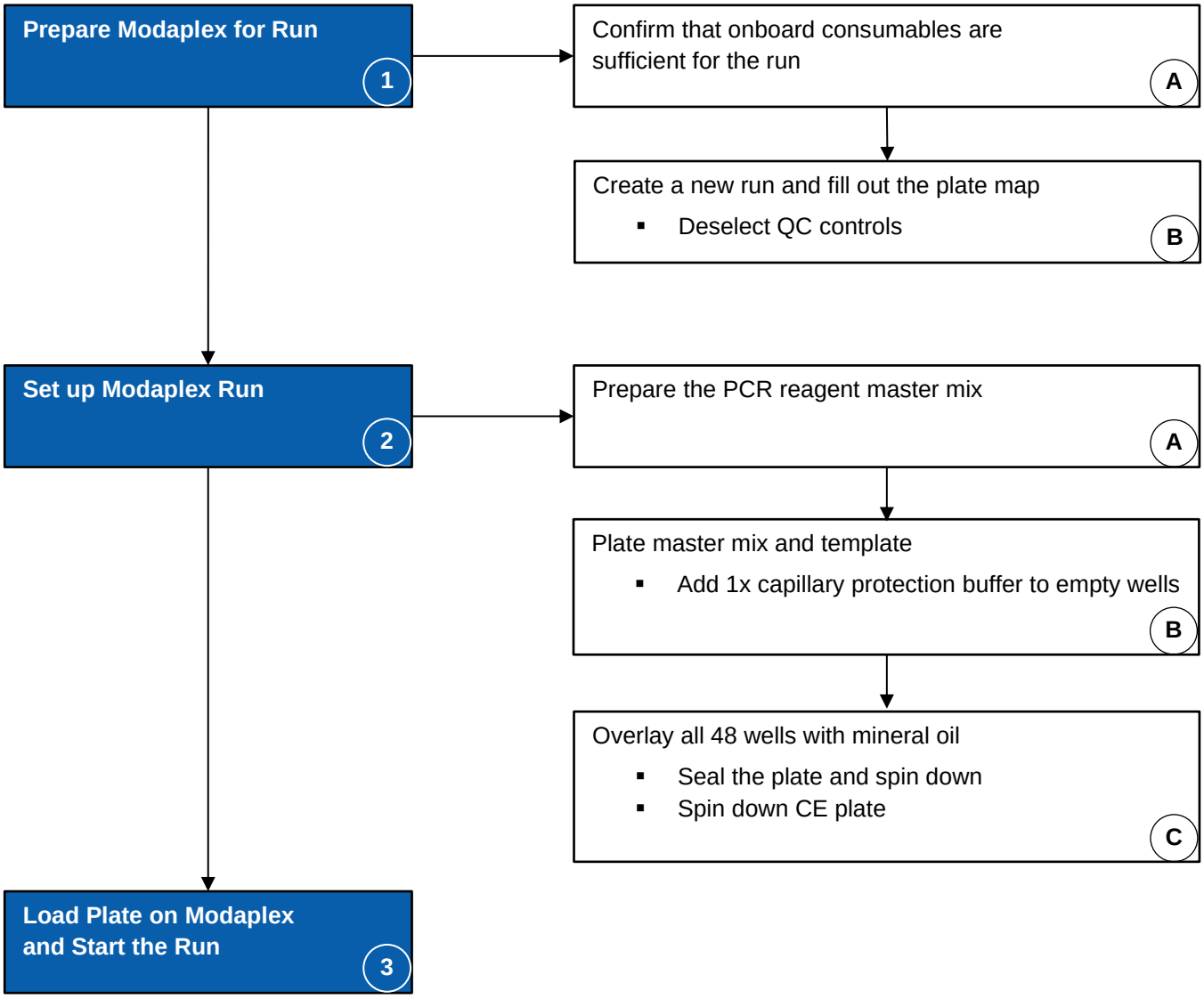


Figure 4: Procedure—Flow Chart

Interpretation of the Results

After the completion of the Modaplex run, the MSI data must be analyzed by the following procedure:

1. Data transfer to the Moda-RA software
2. Data analysis
3. MSI report creation

Data transfer to the Moda-RA software

The following section describes how the MSI data is transferred from the Modaplex system to the Moda-RA software version 1.4.0. or higher.

Before analyzing the Modaplex data for the first time, move the folder containing the Moda-RA software onto your computer. A 64-bit system is recommended. Additionally, a local folder should be created on the computer in which all the Modaplex runs are saved.

Note: The Moda-RA software should not be installed on the Modaplex instrument.

1. **Move** the Modaplex run folder to your analysis computer.

After the completion of the Modaplex run, copy the relative run folder '*RunXXXX*' to an external device and paste it in the folder created on your analysis computer.

Note: The Modaplex instrument creates a run folder related to each Modaplex run, containing all the run-related data. The folder is generated automatically and named with a consecutive number like Run0001, Run0002, or Run003. The relative run folder '*Run0001*' is saved in the folder '*Modaplex Data*', which is present as a shortcut on the desktop of the Modaplex computer.

2. **Open** the Moda-RA software by double-clicking on the Moda-RA.exe file.

3. **Select** *Import Modaplex Run*.

4. **Select** the folder where your run folder is saved and click on it.

5. **Select** *Finish*.

This loads the Modaplex data into the Moda-RA software. The quality control for all wells is performed automatically during import. After the data transfer, the '*Run Overview*' window opens for data analysis.

Data analysis

The following section describes how the Moda-RA software is used for the analysis of the MSI data and how the results are displayed. This section also contains detailed information about the result interpretation of the control and the sample wells, including the comments and recommendations for all possible results. This section is divided into the following subsections:

A. Run overview
B. Sample plate summary and general display of analyzed data
C. Quality control: Analysis of the NC and PC
D. Result interpretation: Analysis of the sample wells
E. Result interpretation: Analysis of the sample wells in detail

A. Run overview

The window *"Overview*" opens automatically after the data import is completed. It contains the Modaplex-related run information such as run ID, run name, start of run, end of run, and the Modaplex instrument identifier. In addition, the Moda-RA configuration identifier is displayed along with the associated assay. All assays present on the plate are displayed. Please refer to Figure 5 for an example.

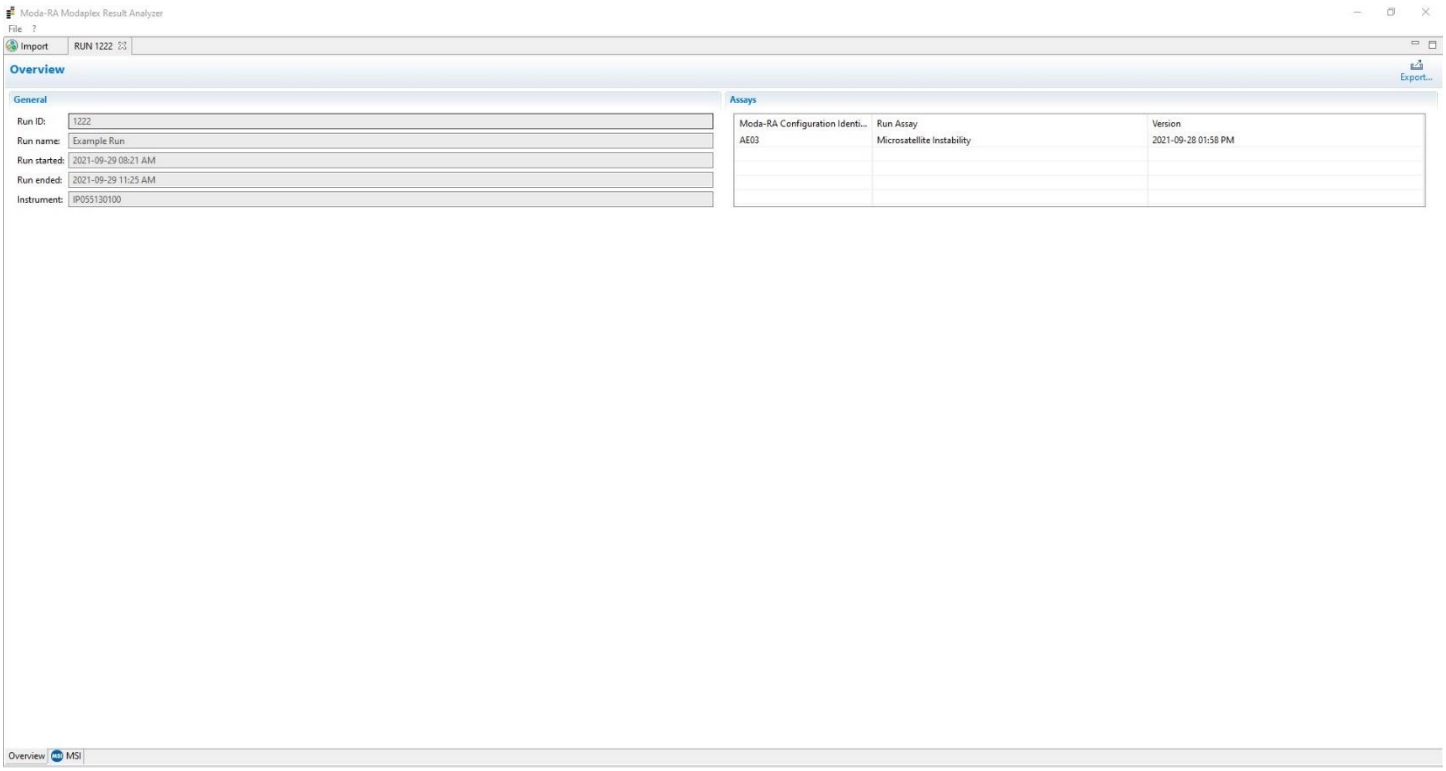


Figure 5: Example of the 'Run Overview' window.

B. Plate summary and general display of the analyzed data

The '*Microsatellite Instability—Plate Summary*' window opens when selecting '*MSI*' in the '*Run Overview*' window. It displays all controls and samples present on the plate that has been imported into the Moda-RA software.

A color code is used to display the validity of each well. The applied color code displays the following information:

1. QC information: Independent determination of the validity of each well
2. Internal control information: The number of the detected internal controls, regardless of allelic heterogeneity

The plate summary is illustrated in Figure 6. The color code is explained in detail in Figure 7.

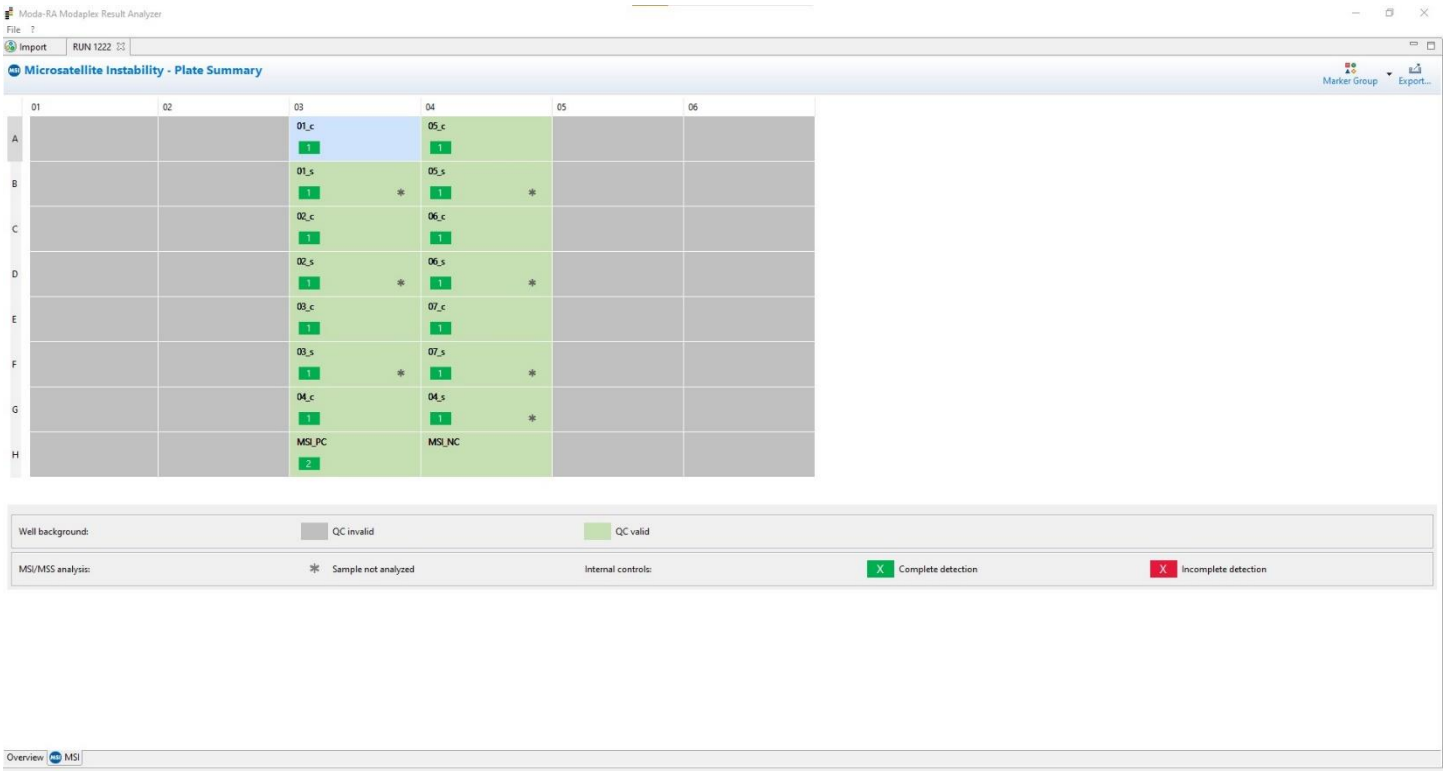
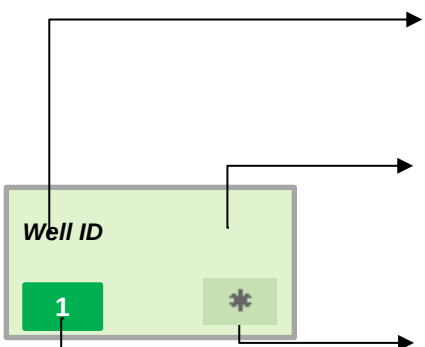


Figure 6: Illustration of the plate summary.

Note: All wells are reported except the empty wells.

Note: If another assay is set up and run on the same PCR plate, the results are shown in a separate tab.



Well ID
Displays affiliation of the well
- Sample well
- Positive control well
- Negative control well

QC information: Background color
Displays the validity of the well
- Green = Valid well
- Grey = Invalid well

MSI/MSS analysis: Overall Evaluation
Displays the MSI/MSS analysis status of the sample pair (displayed on_s)
- with asterisk = Sample not analyzed
- without asterisk = Sample analyzed

Target information: Internal Controls
Displays the number of the detected internal controls
- Green = Complete detection (internal control HLD133 detected)
- Red = Incomplete detection (internal control HLD133 not detected)

Figure 7: Explanation of the Moda-RA color code for sample well

Note: For MSI data analysis, the sample wells have to be marked according to the following code:

Tumor tissue (= sample): *sample name_s*

Normal adjacent tissue (= control): *sample name_c*

Note: Detailed information on the interpretation of the control and the sample wells is given in Tables 5–8.

The '*Microsatellite Instability—Plate Summary*' displays a button labelled **'Marker Group'** above the plate map. By clicking onto this button, the marker group of your interest can be selected. Each marker group displays an individual MSI-H assessment option based on selected Marker Group `Mono- and Dinucleotide Markers´ or ` Mononucleotide Markers ´.

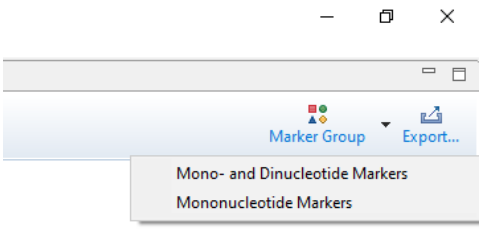


Figure 8: Illustration of the Toolbar 'Marker Group'

C. Quality control: Analysis of the NC and PC

Each Modaplex MSI run should include the run controls NC and PC. A Modaplex run is valid if the PC and the NC runs are valid. The results of the run controls are displayed through changes in the background color of each well on the plate summary.

Note: The validity of the run controls is not connected with the validity of the sample wells. A sample well can be valid even when there are invalid run controls. In such a case, the reason behind the invalid controls should be investigated. Biotype GmbH should be contacted for technical support, if required.

1. Negative Control (NC)

The NC is reported as valid if no internal control (HLD marker) is detected. It is reported as invalid if at least one internal control is detected. Please review the Biotype GmbH troubleshooting guide in case of a failed NC.

Note: For more detailed information, please refer to Tables 5 and 6.

2. MSI Positive Control (PC)

The PC is shown as valid if all markers and internal controls are detected. If the PC fails, the user should review the PC by consulting the Biotype GmbH support.

Note: Please refer to Tables 5 and 6 for detailed information on the criteria for valid or invalid run controls.

Table 5: Moda-RA: Valid and invalid run controls

Background color of control wells	Description	Criteria
	• Valid Modaplex run for PC and NC wells	• At least 2 out of 3 calibrator peaks in FAM or TYE channel detected in NC or PC (calibrator peak C110 (FAM) and C113 (TYE) must be present) • All markers detected in PC • Both HLD131 and HLD133 are detected in PC • No markers detected in NC • No internal controls detected in NC
	• Invalid Modaplex run for PC and NC wells	• Calibrator peak C110 (FAM) or C113 (TYE) not detected in NC or PC • Calibrator peaks C249 and C306 (FAM) or C251 and C309 (TYE) are not detected in NC or PC. • Less than 7 markers detected in PC • Less than two internal controls detected in PC • Detection of any marker in NC • Detection of any internal control in NC

Table 6: Moda-RA software: The information for the run control

Color and number code for the positive control	Description	Criteria
	• Complete detection of internal control	• Displays the two detected internal controls - HLD131 and HLD133
	• Incomplete detection of internal controls	• Displays one detected internal control - HLD131 or HLD133
	• No detection of internal controls	• Internal controls HLD131 and HLD133 not detected

Note: No small boxes are shown for NC wells as no targets or internal controls should be detected.

D. Result Interpretation: Analysis of the sample wells

The '*Microsatellite Instability Panel Summary*' window displays the background colors on the panel summary. The Moda-RA software automatically analyzes the wells and categorizes them as either valid or invalid. Tables 7 and 8 describe the color coding in detail. The wells are characterized according to the number of calibrators and the number of internal controls.

Table 7: Moda-RA software: The QC information for the sample wells

Background Color of sample wells	Description	Criteria
	• Valid sample well	• At least 2 out of 3 calibrator peaks detected (calibrator peak C110 (FAM) and C113 (TYE) must be present) • Internal control HLD133 detected
	• Invalid sample well	• calibrator peak C110 (FAM) or C113 (TYE) not detected • Calibrator peaks C249 and C306 (FAM) or C251 and C309 (TYE) are not detected • Internal control HLD133 not detected

Table 8: Moda-RA software: The information for the run sample wells

Color and number code for the sample wells	Description	Criteria
1	• Detection of internal control	• Internal control HLD133 detected
0	• No detection of internal control	• Internal control HLD133 not detected

To simplify the analysis of the sample pairs, the well of the tumor samples—labelled with _s is shown with a star (*). This label vanishes when the tumor sample is evaluated.

For more information about the well, **move the cursor** above the well.

1. A pop-up window appears, displaying well name and well type.

2. **Double-click** the well of interest to see the electropherograms.

   A tab opens on the right for each well. The marker panel of choice is displayed on the top. Each marker can be evaluated. If there is a corresponding sample -either _s or _c, named identically before the underscore, you can automatically see the overlay of both signals in the electropherograms.

   Note: If the naming of the sample pair is not identical, you can individually overlay the samples by using the following toolbar icon: This will open a pop-up window display all available wells. Please select the well for overlay.

3. By clicking on the marker in the marker panel (Section #1, Figure 9), an automatic zoom into this marker occurs. You can start evaluating each marker immediately.

4. Below the marker panel and the two electropherograms (EPG) are displayed.
The EPG of the FAM channel is displayed in Section #2 and that of the TYE channel in Section #3. The range of each marker is clearly shown. You can individually zoom into each one.

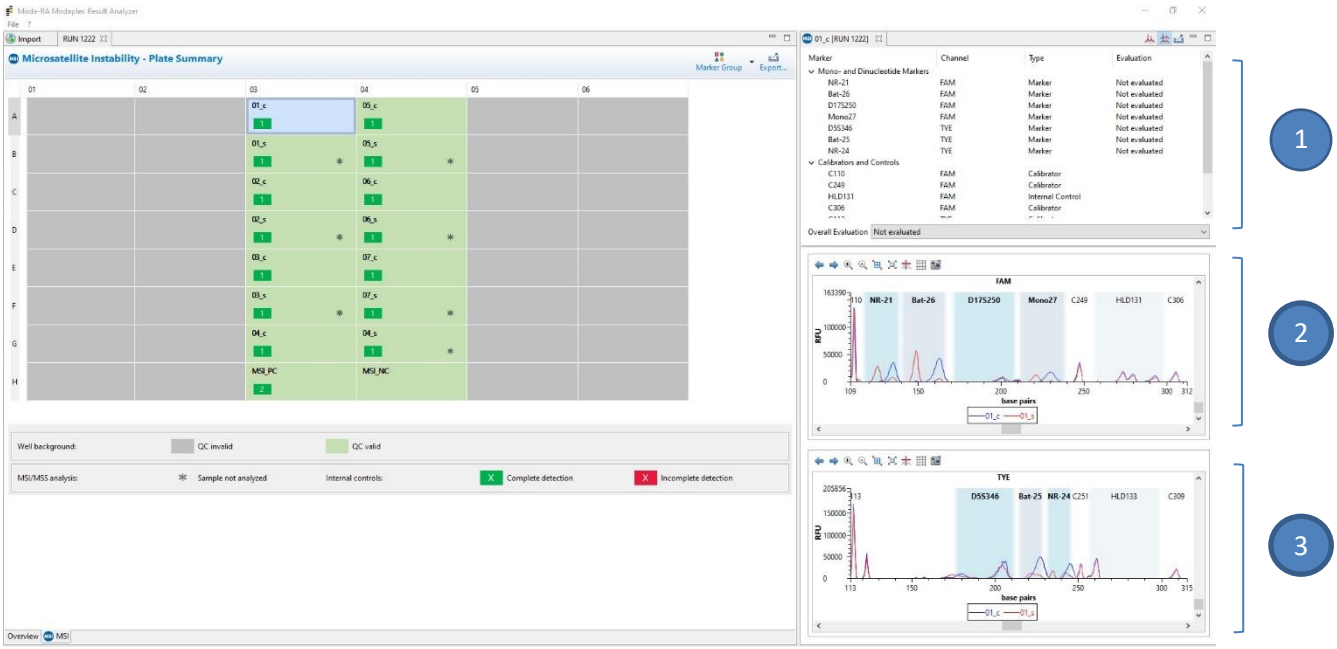


Figure 9: Data analysis of sample wells (the blue numbers show the different sections).

By default, the red line represents the signal of the sample well (_s) and the blue line the signal of the control well (_c). The unit of the Y-axis of the coordinate system is RFU, whereas the shared X-axis displays 'base pairs' (bp).

Note: Technical-issue-related side peaks occur. The bands do not affect the data MSI analysis and are therefore negligible. They are located at the following positions of the Y-axis in the FAM channel and TYE channel: 113 bp (FAM), 127 bp (FAM), ca. 140 bp (FAM), 260 bp (FAM), 273 bp (FAM), 118 bp (TYE), 113-170 bp (TYE), 180 bp (TYE) and 205 bp (TYE)

5. Various toolbar icons (see *Table 9*) are available for different optical presentations of the electropherograms in Sections #4 and #5 (see *Figure 10*).

Note: A full screen version of the electropherogram is available as well.

Figure 10: Moda-RA software: Presentation of electropherograms (the blue numbers show the different sections).

Table 9: Moda-RA software: The toolbar icons of electropherograms.

Icon	Description
	• With the Arrow icons, you can switch between the previous marker and the next marker.
	• Use the buttons “Zoom In” and “Zoom Out” in the electropherogram toolbar.
	• Every part of a coordinate system can be magnified with dynamic zoom. To this end, click with the left mouse button into the representation and draw a frame to the right while keeping the mouse button pressed. Upon releasing the button, the selected area of the coordinate system is magnified. Repeat this procedure as often as you like. To zoom out, press the left mouse button and keep it pressed while drawing the mouse to the left.
	• Full Zoom out brings you back to the complete representation of the EPG.
	• Click Show/Hide Cursor to activate cursor. The lines of the cursor extend to the end of the coordinate system. If several related coordinate systems are depicted one below the other, the vertical cursor is shown in the other coordinate systems as well.
	• A grid is displayed in the EPGs.
	• Take a snapshot and save as PNG file.
	• Maximize electropherogram (FAM and TYE channels).
	• Compare electropherograms (sample and control wells).
	• Export: create a printable report for documentation or export of data.

6. **Select** ‘Stable’, ‘Instable’, or ‘Uncertain’ on the evaluation field in Section #1 after the analysis of electropherograms in Sections #2 and #3.

7. **Repeat** the steps for each marker.

8. **Select** the ‘Overall Evaluation’ field. Click with the left mouse and select ‘MSI-High’, ‘MSI-Low’ or ‘MSS stable’. The asterix on the sample well disappears now.

   Note: Do not close the well tabs before creating a printable report; otherwise, the evaluation will be lost.

E. Result Interpretation: Analysis of the sample wells in detail

Before the MSI status can be evaluated in the Moda-RA software version 1.4.0 and higher, it is necessary to confirm the correct match of control well (native) and sample well (tumor) in the electropherograms. The red line represents the signal of the sample well (_s) and the blue line the signal of the control well (_c). The calibrator (control) peaks C110 (FAM) and C113 (TYE) of the blue and red line must be aligned and should be of similar height. In addition, the internal control peaks HLD131 and HLD133 must be congruent in order to confirm the correct alignment of the diagram and the patient identity.

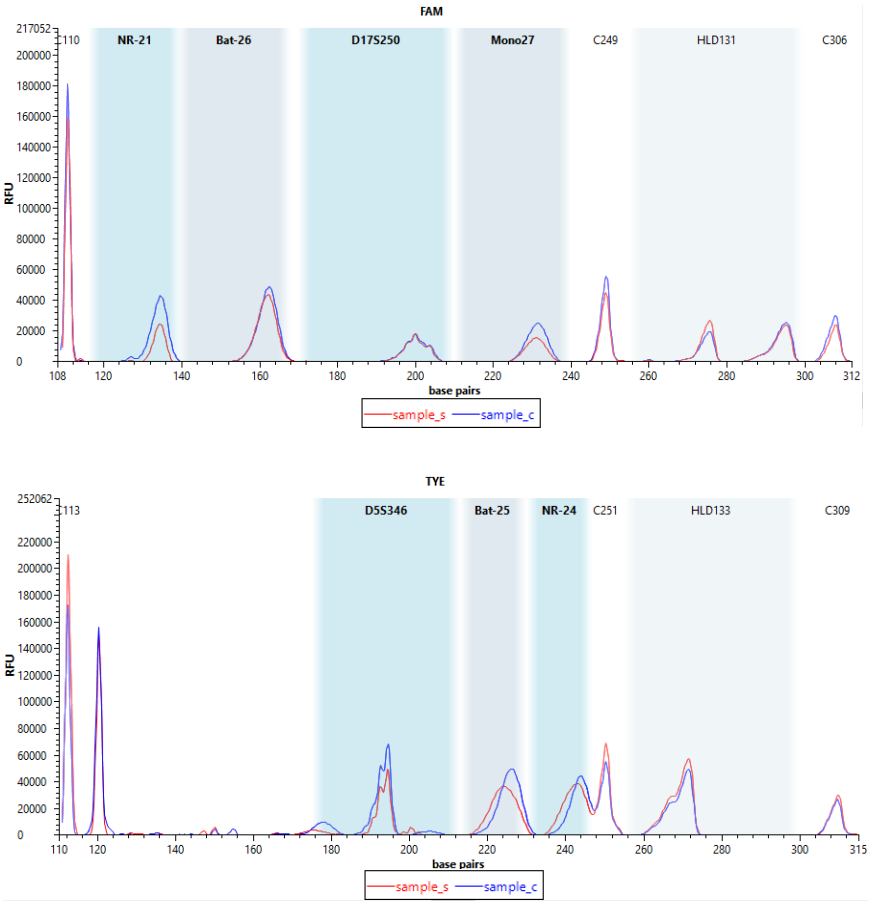


Figure 11: Moda-RA software: Presentation of electropherograms with correct assignment.

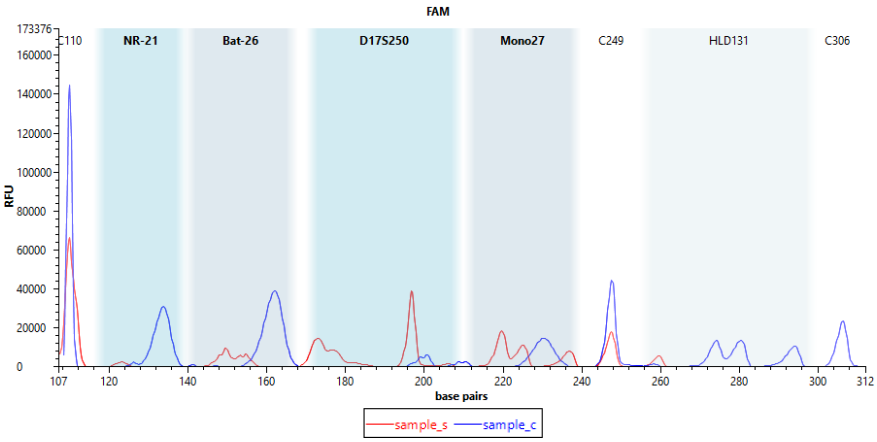


Figure 12: Moda-RA software: Presentation of electropherogram with C110 misassignment.

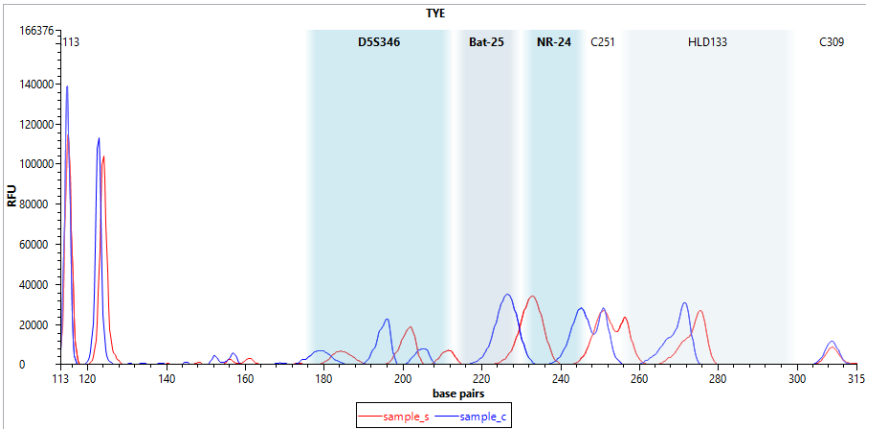


Figure 13: Moda-RA software: Presentation of electropherogram with HLD133 misassignment.

Note: If you recognize one of these misassignment, please contact our support team.

In order to simplify the analysis of the sample pairs, examples for the visual representation of the individual mono- and dinucleotides in the electropherogram are shown in the next section. The visual representations are only examples of the status “Stable" or "Instable” and are an orientation aid for the evaluation.

Note: Two criteria shall be applied for characterisation of instable targets. If one or both of the criteria are met, the respective target can be judged as instable.

1. Shift of the whole peak. Please refer to the maximum of the individual peaks and assess whether migration length of tumor signal and native adjacent tissue signal differs by at least 2 bp. Peak height differences can occur and shall not be the basis for the evaluation.

2. Emergence of a second peak maximum. The original peak can persist in this case and a new maximum arises. It is possible that instability manifests as a shoulder of the original peak or as a new signal.

No signals below 3000 RFU shall be considered for evaluation. Only for the targets D17S250 and Mono27, signals may be as low as 1000 RFU. Signals below 1000 RFU shall be ignored.

Note: If it cannot be clearly assessed whether one of the two criteria applies, the rating “uncertain“ should be assigned. It is recommended to repeat the run if two or more markers are evaluated as “uncertain“. In case of repetition, an increased DNA input of 20 ng should be used.

Table 10: Visual orientation of evaluation of "Stable" and "Instable" status of Marker NR-21

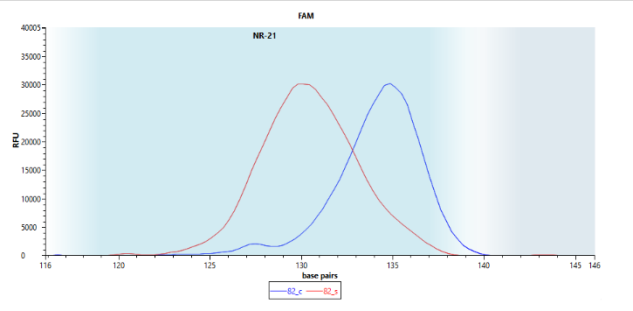
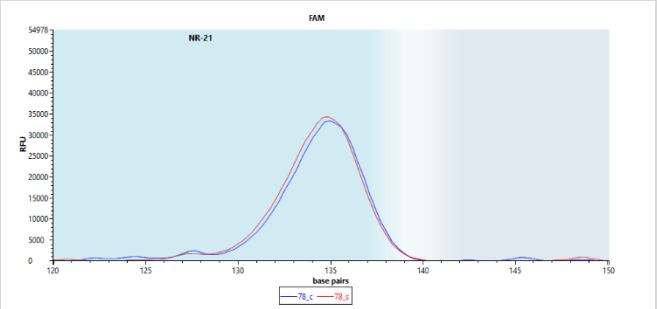
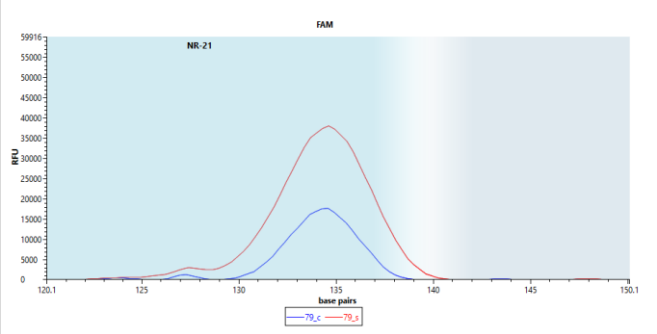
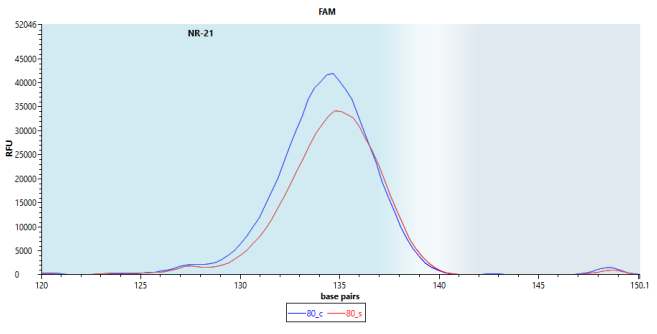
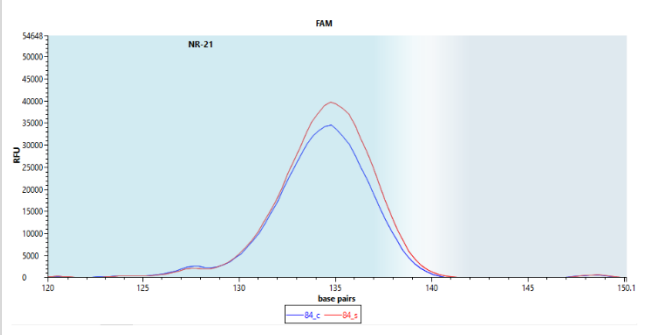
Mononucleotide Marker NR-21	
MSI "Instable "	MSS "Stable"
	
	
	
	

Table 11: Visual orientation of evaluation of "Stable" and "Instable" status of Marker Bat-26

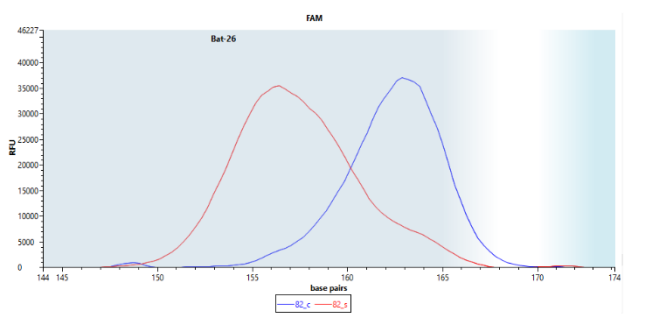
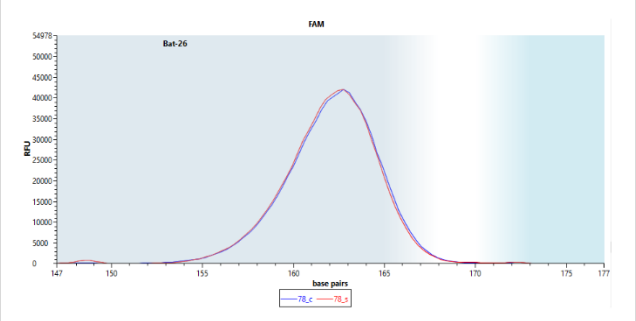
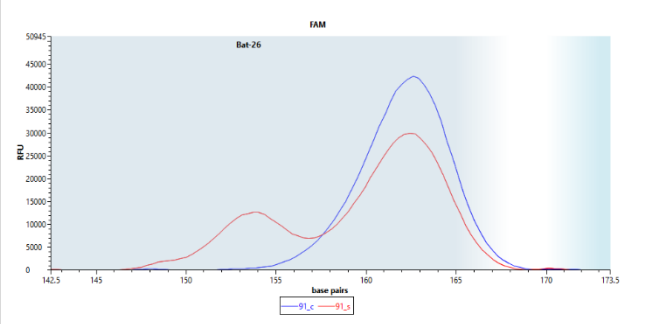
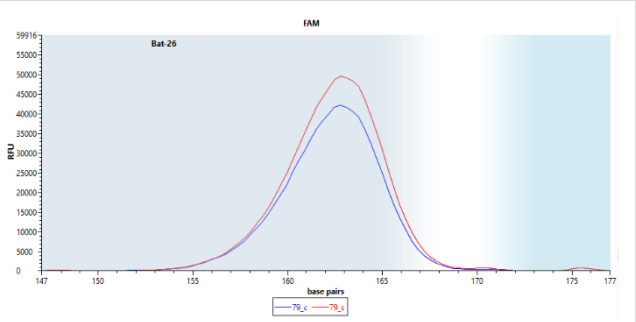
Mononucleotide Marker Bat-26	
MSI "Instable "	MSS "Stable"
	
	

Table 12: Visual orientation of evaluation of "Stable" and "Instable" status of Marker D17S250

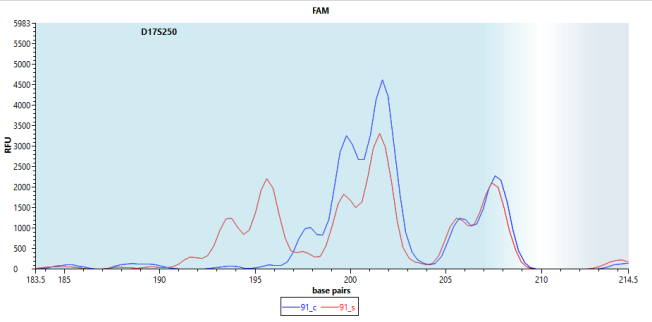
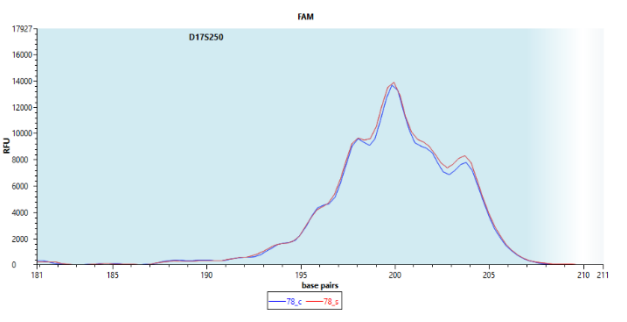
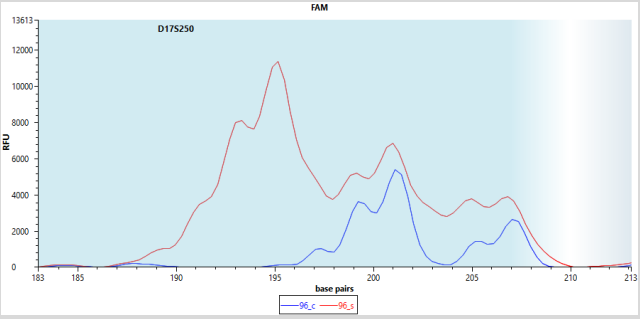
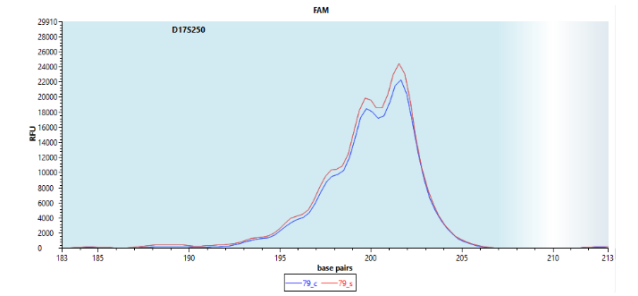
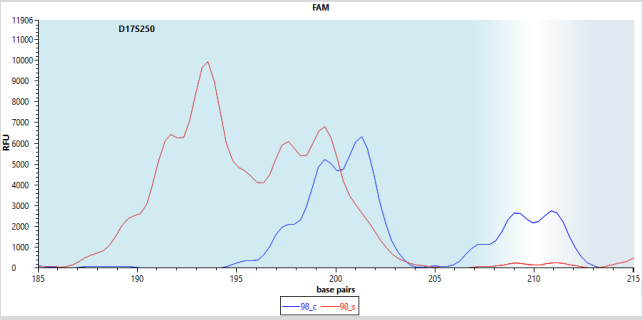
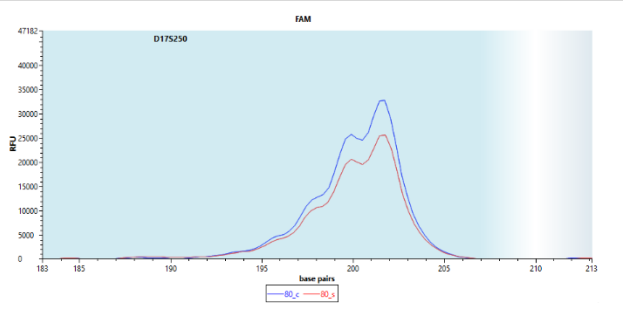
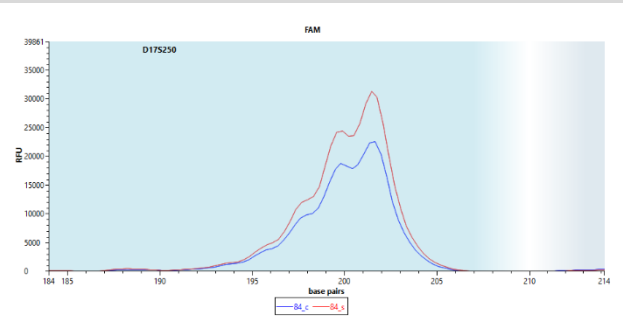
Dinucleotide D17S250	
MSI "Instable "	MSS "Stable"
	
	
	
	

Table 13: Visual orientation of evaluation of "Stable" and "Instable" status of Marker Mono27

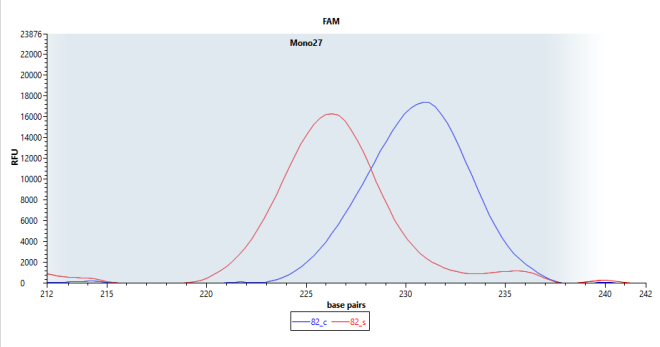
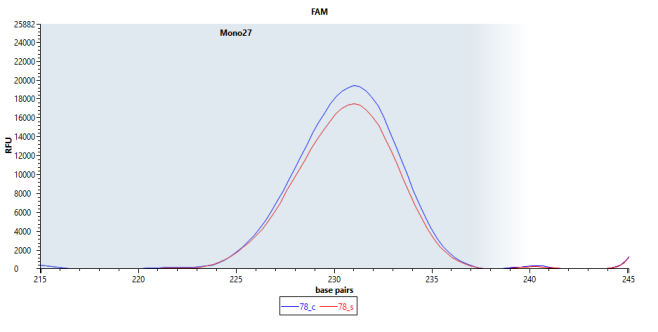
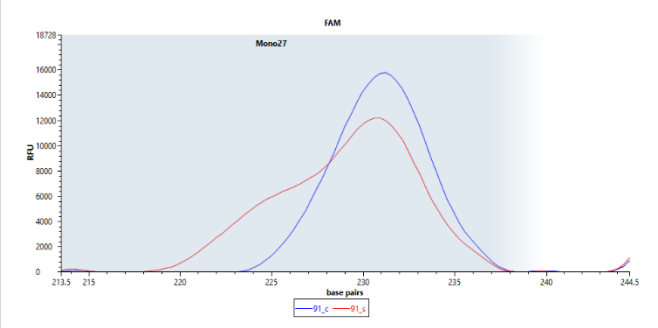
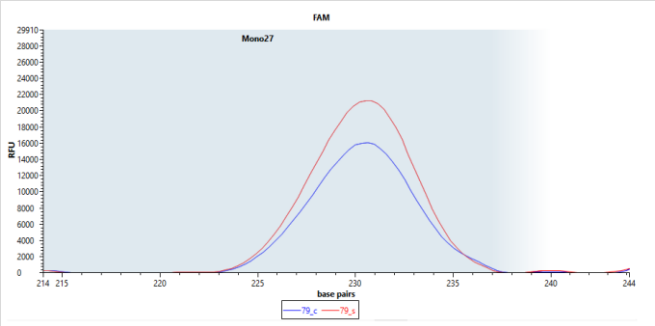
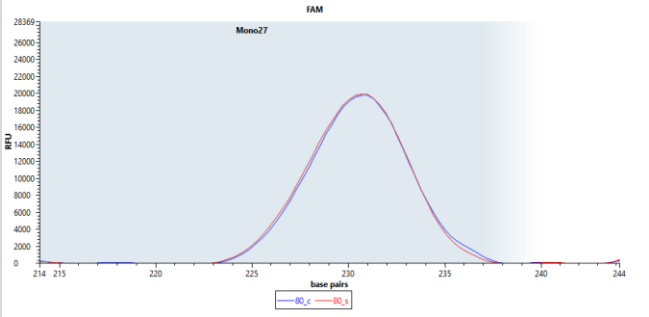
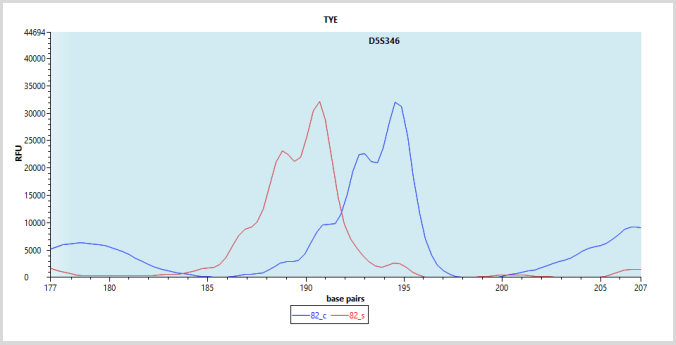
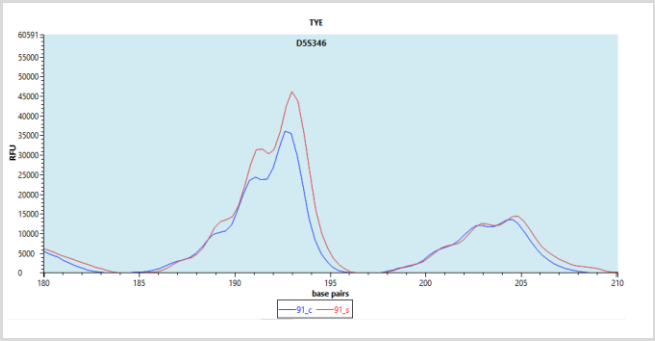
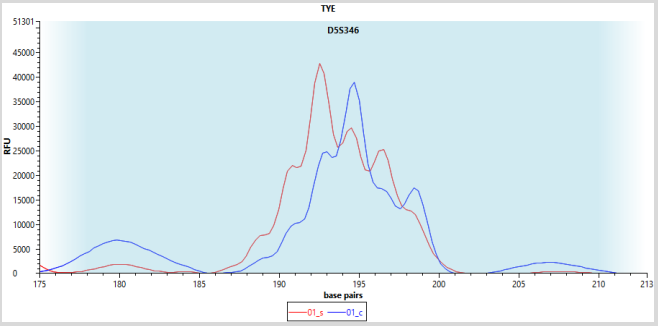
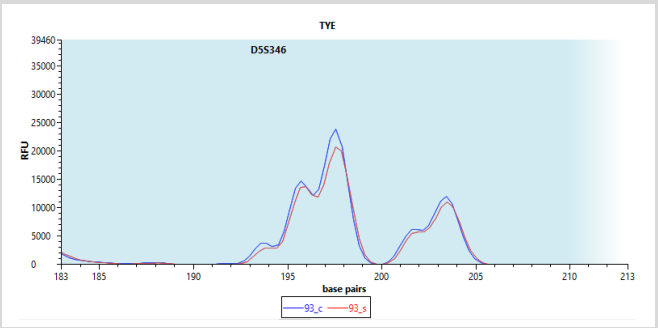
Mononucleotide Mono27	
MSI "Instable "	MSS "Stable"
	
	
	

Table 14: Visual orientation of evaluation of "Stable" and "Instable" status of Marker D5S346

Dinucleotide D5S346	
MSI "Instable "	MSS "Stable"
	
	

Note: This target region includes known side products that can appear left and right of the D5S346 signal. They can be easily distinguished from the spiky marker signal as they are flat and smooth. These side products should never be the basis for evaluation of D5S346 stability or instability.

Table 15: Visual orientation of evaluation of "Stable" and "Instable" status of Marker Bat-25

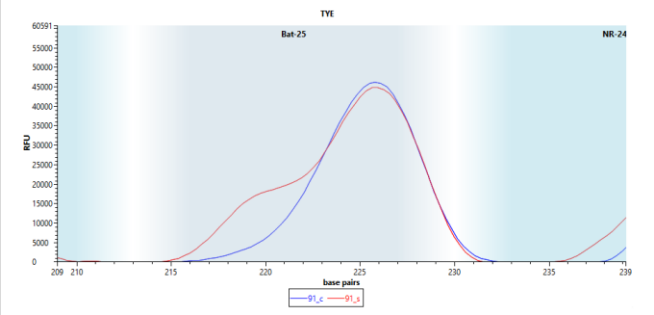
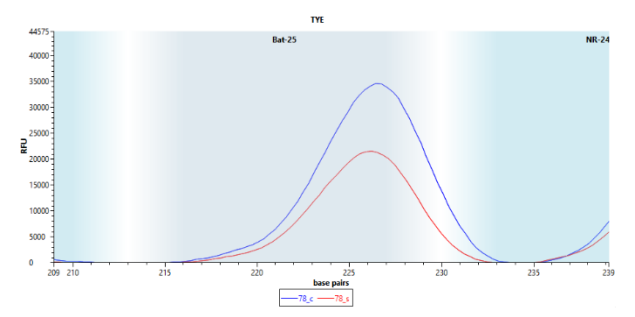
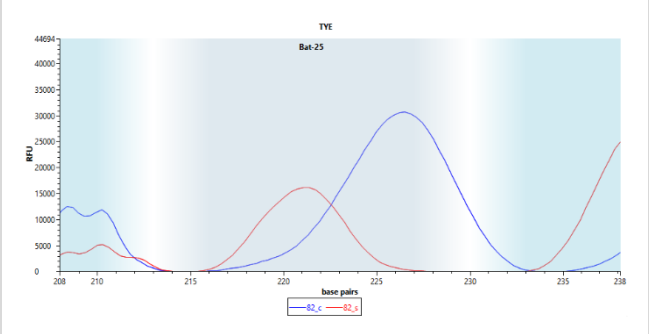
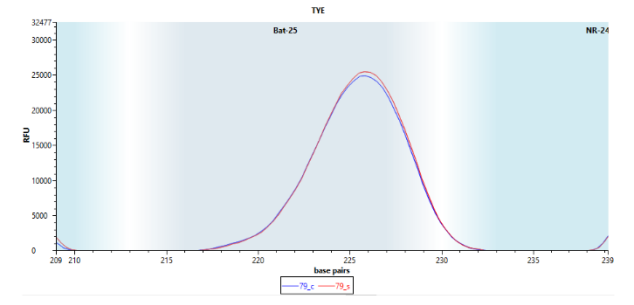
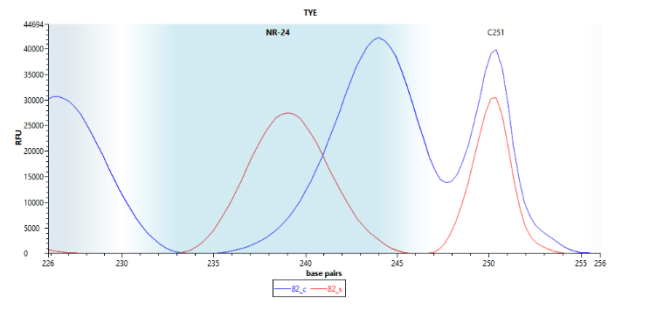
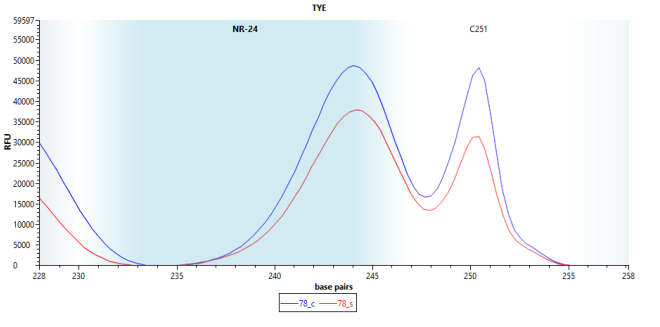
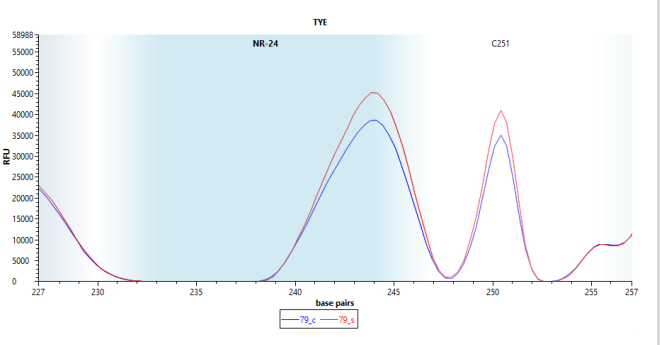
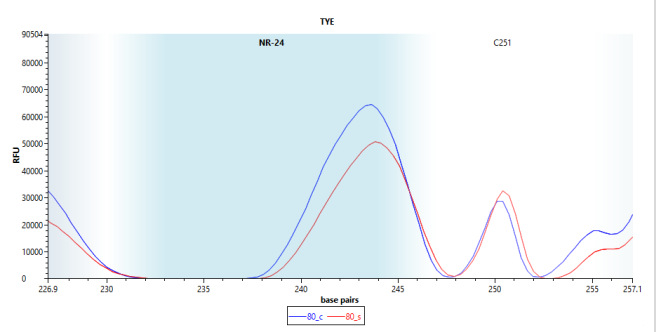
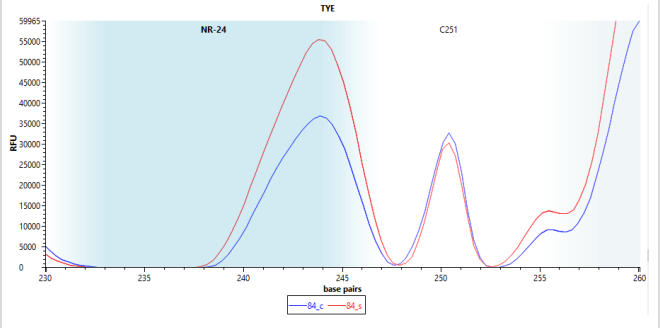
Mononucleotide Bat-25	
MSI "Instable "	MSS "Stable"
	
	

Table 15: Visual orientation of evaluation of "Stable" and "Instable" status of Marker NR-24

Mononucleotide NR-24	
MSI "Instable "	MSS "Stable"
	
	
	
	

Creating the MSI report

This protocol is for the preparation of a report after the MSI data has been analyzed and classified as valid. The report contains the following information:

- The result of the sample
- Sample information
- Modaplex MSI Analysis Kit information, such as lot, assay ID, and expiration date
- Information on the Modaplex run, including consumable lots

For creating the MSI report and exporting the report as a *.pdf file, the user should follow the instructions below:

1. **Select** *File* on the Toolbar of the '*Plate Summary*' window and click *Export.*

2. **Select** *Create a Printable Report* and then select *Next*.

3. **Choose** a file export destination.

   In this window, it is possible to include the calibrator lot number in the report.

4. **Select** *Finish.*
   A *.pdf file is created automatically.

For creating the MSI report and exporting the report as a *.csv file, the user should follow the instructions below:

1. **Select** *File* on the Toolbar of the '*Plate Summary*' window and click on *Export.*

2. **Select** *Export to files* and then select *Next*.
   Now you can choose from various csv-format options as well as the sylk-format.

3. **Choose** a folder where you want to save your file.

4. **Select** *Finish.*
   The file is created automatically

   Note: The document will be automatically named `*Microsatellite Instability*` and should be renamed after saving.

Performance Characteristics

Table 8. Performance characteristics of the Modaplex MSI Analysis Kit

Assay Performance	Result/ Description
Primer Specificity	A basic local alignment search tool (BLAST) analysis was performed. The primer of the Modaplex MSI Analysis Kit only amplifies seven targets (Bat-25, Bat-26, NR-21, NR-24, Mono27, D5S346, D17S250) and two internal control targets (HLD131 and HLD133).
Sample Material	The Modaplex MSI Analysis Kit has been verified with human gDNA and DNA samples extracted from formalin-fixed, paraffin-embedded (FFPE) colorectal cancer (CRC) tissue. In addition, DNA samples extracted from formalin-fixed paraffin-embedded (FFPE) endometrial tissue have been tested for use with the Modaplex MSI Analysis Kit.
Input	10 ng (2 ng/µL)
Freeze Thaw Stability	Store all components at -25 °C to -15 °C and avoid repeated thawing and freezing. The Modaplex MSI analysis kit is verified to be stable for 5 freeze-thaw cycles.

Troubleshooting Guide

The troubleshooting guide may be helpful for solving any problems that may arise. Also, see the Modaplex System User Manual for Instrument and Software Troubleshooting Guidance. The Biotype GmbH are happy to answer any questions about the information and protocols given in the IFU (for contact information, see the back cover).

Failure	Comments and suggestions
Invalid negative control (_NC)	• Targets and/or internal controls were detected in NC. Contamination occurred during the preparation of the PCR. Repeat the PCR with new reagents in replicates. If possible, close the PCR tubes directly after addition of the sample to be tested. Do not reseal the plates with the same plate seal. Ensure that the workspace and the instruments are decontaminated at regular intervals. • Check the maintenance interval for all used devices (e.g., pipettes) • NC well was not labeled properly (i.e., NC instead of _NC). Check your Modaplex plate map and modify if necessary. After this, re-analyze and load again into Moda-RA. Please make sure that no “spaces” occur after _NC when setting up the plate map.
Invalid positive control (_PC)	• Incomplete detection of targets, calibrators and/or internal control. Incorrect handling occurred during the preparation of the PCR and/or positive control. Repeat the PCR with new reagents in replicates. If possible, close the PCR tubes directly after addition of the sample to be tested. Do not reseal the plates with the same plate seal. Ensure that the workspace and the instruments are decontaminated at regular intervals. • Check the maintenance interval for all used devices (e.g., pipettes) • PC well was incorrectly labeled (i.e., PC instead of _PC). Correct the name of the well in the plate set-up on the Modaplex and re-analyze the run. Please make sure that no “spaces” occur after _PC when setting up the plate map.
The storage conditions for one or more kit components do not comply with the instructions given in ‘Reagent Storage and Handling Conditions’ on p. 6	• Check the storage conditions and the expiration date (see the kit label). Please use a new kit if the reagents were stored improperly.
The Modaplex MSI Analysis Kit past the expiration date	• Check the storage conditions and the expiration date (see the kit label). Please use a new kit if the kit or any kit component is past the expiration date.
Incorrect overlay of peaks.	• Calibrators have failed or assigned incorrectly. Please contact technical support.
Targets only present in one channel	• Review all the run controls and the sample wells in the Moda-RA software. If no well shows fluorescence in one channel, contact Biotype GmbH

Limitations

All results obtained with the product must be interpreted within the context of all relevant laboratory findings. The results are not to be used for diagnosis.

The product is to be used only by specifically instructed personnel who have been properly trained to use the Modaplex platform.

The product is intended for use with the Modaplex platform only.

For optimal results, strict compliance with the Modaplex MSI Analysis Kit IFU is required. The dilution of the reagents, other than as described in this IFU, is not recommended and will result in a loss of performance.

It is important that the amount and quality of the DNA in the sample are assessed prior to performing a sample analysis using the Modaplex MSI Analysis Kit.

Attention should be paid to expiration dates and storage conditions printed on the box and on the labels of all components. Do not use expired or incorrectly stored components.

Warranties and Disclaimer

This product is warranted to perform as described when used in strict conformity with the instructions herein. The product has been designed for research use only and is to be used solely by qualified professionals. It is the user's responsibility to ensure that a given product is suitable for a given application.

Biotype GmbH provides no other warranty, expressed or implied, and disclaims any implied warranty of merchantability or fitness for a particular purpose. Under no circumstances whatsoever shall Biotype GmbH be liable for any indirect, special, or consequential damages.

References

[1] P. Peltomaki, "Role of DNA mismatch repair defects in the pathogenesis of human cancer", J Clin Oncol, vol. 21, pp. 1174–1179, 2003

[2] M.F. Kane, M. Loda, G.M. Gaida, J. Lipman, R. Mishra, H. Goldman, J.M. Jessup, R. Kolodner, "Methylation of the hMLH1 promoter correlates with lack of expression of hMLH1 in sporadic colon tumors and mismatch repair-defective human tumor cell lines.", Cancer Res. vol. 57, pp. 808–811, 1997

[3] G.M. Losso, R. Moraes, A.C. Gentili, I.T. Messias-Reason, "Microsatellite Instability—MSI Markers (BAT26, BAT25, D2S123, D5S346, D17S25) in Rectal Cancer.", ABCD Arq Bras Cir Dig. Vol. 25(4), pp. 240–244, 2012

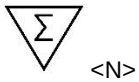
[4] "Revised Bethesda Guidelines for Hereditary Nonpolyposis Colorectal Cancer (Lynch Syndrome) and Microsatellite Instability", J Natl Cancer, vol. 96(4), pp. 261–268, 2004.

Symbols

The following symbols may appear on the packaging and labelling:

Manufacturer

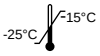
Batch code



Contains sufficient for <N> tests

consult electronic instructions for use

Use-by date



Temperature limit

Catalogue number

Keep away from sunlight

Keep dry

Technical Support

For technical support or information, please call Biotype GmbH at +49-(0)351-8838 400.

Contact Information

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01109 Dresden

Germany

Phone: +49-(0)351-8838 400

Fax: +49-(0)351-8838 403

Email: support@biotype.de

Ordering Information

Product	Contents	Cat. no.
Modaplex MSI Analysis Kit	For 50 reactions: MSI Primer Mix, PCR Buffer 10, Modaplex Polymerase P, MSI Positive Control, Modaplex Calibrator 2, Nuclease-Free Water *Not available in Italy and United States of America (USA)	85-10701-0050*
Modaplex and Consumables		
Modaplex System	Modaplex Instrument, Monitor, Barcode Reader Kit, PC Keyboard, PC Mouse, Printer, Cables, 1 Modaplex TC Hold -down Plate, 1 Modaplex Cartridge with 48 Capillaries	00-04901-0001
Modaplex TC Hold-down Plate	1 Modaplex TC Hold-down Plate	00-04X01-0001
Modaplex 48 Capillary Cartridge	1 Modaplex Cartridge with 48 Capillaries	00-14X02-0001
Modaplex Buffer	2 Bottles of Modaplex Buffer	00-14302-2000
Modaplex Decon	2 Bottles of Modaplex Decon	00-14303-2000
POP-7/ Modaplex CE Gel	1 Bottle of Modaplex CE Gel	00-04305-0028
Modaplex Wash	1 Bottle of Modaplex Wash	00-14304-0250
Modaplex CE Plates	1 Box of 20 Modaplex CE Plates	00-14306-0020
Mineral Oil	5 Bottles of Mineral Oil	00-04301-0025
10X Capillary Protection Buffer Kit	3 Tubes 10X Capillary Protection Buffer (1.5 mL each)	85-21001-1800
PCR Microplates 96	1 Box of 25 96-well PCR Plates	00-14X03-0025
Aluminium Sealing Film	1 Box of 100 Aluminium Sealing Film	00-14X04-0100

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