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Viral RNA/DNA isolation

User manual

NucleoMag® Virus

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Viral RNA/DNA isolation

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1 Components

1.1 Kit contents

	NucleoMag [®] Virus	
REF	1x 96 preps 744800.1	4 x 96 preps 744800.4
NucleoMag® V-Beads	2 x 1.5 mL	12 mL
Lysis Buffer MVL	2 x 13 mL	125 mL
Binding Buffer MV2	75 mL	300 mL
Wash Buffer MV3	75 mL	300 mL
Wash Buffer MV4	75 mL	300 mL
Wash Buffer MV5	60 mL	250 mL
Elution Buffer MV6	13 mL	60 mL
Carrier RNA*	400 μg	4 x 400 μg
Carrier RNA Buffer	500 μL	4 x 500 μL
Proteinase K (lyophilized)*	20 mg	4 x 20 mg
Proteinase Buffer PB	1.8 mL	8 mL
User manual	1	1

^{*} For preparation of working solutions and storage conditions see section 3.

1.2 Material to be supplied by user

Product	REF	Pack of
Separation plate for magnetic beads separation, e.g., Square-well Block (96-well block with 2.1 mL square-wells)	740481 740481.24	4 24
Lysis tubes for incubation of samples and lysis, e.g., Rack of Tubes Strips (1 set consists of 1 Rack, 12 Strips with 8 tubes (1.2 mL wells) each, and 12 Cap Strips)	740477 740477.24	4 sets 24 sets
Elution plate for collecting purified nucleic acids, e.g., Elution Plate U-bottom (96-well 0.3 mL microtiterplate with 300 μ L u-bottom wells) e.g., Elution Plate Flat-bottom (96-well 0.3 mL microtiterplate with 300 μ L flat-bottom wells)	740486.24 740673	24 20
For use of kit on KingFisher® Flex instrument: KingFisher® Accessory Kit A (Square-well Blocks, Deep-well Tip Combs, Elution Plates for 4 x 96 NucleoMag® Virus preps using KingFisher® Flex platform)	744950	1 set
For use of kit on KingFisher® Duo/Duo Prime instrument: KingFisher® Duo Accessory Kit (KingFisher® Deep-well Blocks, KingFisher® Duo 12 Tip Combs, KingFisher® Duo Elution Strips for 8 x 12 NucleoMag® Virus preps using KingFisher® Duo/Duo Prime platform)	744952	1 set

2 Product description

2.1 The basic principle

The **NucleoMag® Virus** kit is designed for the isolation of viral DNA or RNA from cell-free body fluids such as serum or plasma. This kit provides reagents and magnetic beads for isolation of 96 samples from 200 μL serum or plasma. The procedure is based on the reversible adsorption of nucleic acids to paramagnetic beads under appropriate buffer conditions. Sample lysis is achieved by incubation with a new and improved Lysis Buffer MVL containing chaotropic ions supported by Proteinase K digestion. For binding of nucleic acids to the paramagnetic beads, Binding Buffer MV2 and the NucleoMag® V-Beads are added to the lysate. After magnetic separation, the paramagnetic beads are washed to remove contaminants and salts using Wash Buffers MV3 and MV4. Residual ethanol from previous wash steps is removed by a short incubation of the beads in Wash Buffer MV5. Finally, highly pure viral RNA/DNA is eluted with low salt Elution Buffer MV6 or water. Purified viral RNA/DNA can directly be used for downstream applications. The **NucleoMag® Virus** kit can be used either manually or automated on standard liquid handling instruments or automated magnetic separators.

2.2 Kit specifications

NucleoMag® Virus is designed for rapid manual and automated small-scale preparation of viral RNA/DNA from cell-free body fluids such as serum or plasma samples. The kit is designed for use with NucleoMag® SEP magnetic separator plate (see ordering information) or other magnetic separation systems (see section 2.3). Manual time for the preparation of 96 samples is about 120 minutes. The purified RNA/DNA can be used directly as template for RT-PCR, PCR, or any kind of enzymatic reactions.

NucleoMag® Virus allows easy automation on common liquid handling instruments or automated magnetic separators. The actual processing time depends on the configuration of the instrument and the magnetic separation system used. Typically, 96 samples can be purified in less than 120 minutes using the NucleoMag® SEP on the automation platform.

2.3 Magnetic separation systems

For use of **NucleoMag® Virus**, the use of the magnetic separator NucleoMag® SEP is recommended. Separation is carried out in a Square-well Block (see ordering information). The kit can also be used with other common separators.

Magnetic separator	Separation plate or tube
NucleoMag [®] SEP (MN REF 744900)	Square-well Block (MN REF 740481)
Tecan Te-MagS™	1.5 mL tubes without lid (Sarstedt)

Static magnetic pins

Separators with static magnetic pins, for example, NucleoMag® SEP (for manual use and for use on liquid handling workstations): This type of separator is recommended in combination with a suitable microplate shaker for optimal resuspension of the beads during the washing and elution steps. Alternatively, beads can be resuspended in the buffer by pipetting up and down several times. For fully-automated use on liquid handling workstations, a gripper tool is required, the plate is transferred to the magnetic separator for separation of the beads and transferred to the shaker module for resuspension of the beads.

Movable magnetic systems

Separators with moving magnetic pins: Magnetic pins/rods are moved from one side of the well to the other and vice versa. Beads follow this movement and are thus pulled through the buffer during the wash and elution steps. Separation takes place when the system stops.

Automated separators

Separators with moving magnets: Magnetic beads are transferred into suitable plates or tubes. Beads are resuspended from the rod-covered magnets. Following binding, washing or elution beads are collected again with the rod-covered magnets and transferred to the next plate or tube.

2.4 Adjusting the shaker settings

When using a plate shaker for the washing and elution steps, the speed settings have to be adjusted carefully for each specific separation plate and shaker to prevent cross-contamination from well to well. Proceed as follows:

Adjusting shaker speed for binding and wash steps:

- Load 1000 μL (for checking the settings for the binding step) or 600 μL (for checking the settings for the washing steps) dyed water to the wells of the separation plate. Place the plate on the shaker and start shaking with a moderate speed setting for 30 seconds. Turn off the shaker and check the plate surface for small droplets of dyed water.
- Increase speed setting, shake for an additional 30 seconds, and check the plate surface for droplets again.
- Continue increasing the speed setting until you observe droplets on top of the separation plate. Reduce speed setting, check again, and use this setting for the washing step.

Adjusting shaker speed for the elution step:

 Load 100 µL dyed water to the wells of the collection plate and proceed as described above.

2.5 Handling of beads

Distribution of beads

A homogeneous distribution of the magnetic beads to the individual wells of the separation plate is essential for a high well-to-well consistency. Therefore, before distributing the beads, make sure that the beads are completely resuspended. Shake the storage bottle well or place it on a vortexer shortly. Premixing magnetic beads with the binding buffer allows easier homogenous distribution of the beads to the individual wells of the separation plate. During automation, a premix step before aspirating the beads/binding buffer mixture from the reservoir is recommended to keep the beads resuspended.

Magnetic separation time

Attraction of the magnetic beads to the magnetic pins depends on the magnetic strength of the magnetic pins, the selected separation plate, distance of the separation plate from the magnetic pins, and the volume to be processed. The individual times for complete attraction of the beads to the magnetic pins should be checked and adjusted on each system. It is recommended using the separation plates or tubes specified by the supplier of the magnetic separator.

Washing the beads

Washing the beads can be achieved by shaking or mixing. In contrast to mixing by pipetting up and down, mixing by shaker or magnetic mixing allows simultaneous mixing of all samples. This reduces the time and number of tips needed for the preparation. Resuspension by pipetting up and down, however, is more efficient than mixing by a shaker or magnetic mix.

Method	Resuspension efficiency	Speed	Number of tips needed
Magnetic mix	+	++	Low
Shaker	++	++	Low
Pipetting	+++	+*	High

2.6 Elution procedures

Purified viral RNA/DNA can be eluted directly with the supplied Elution Buffer MV6. Elution can be carried out in a volume of $\geq 50~\mu L$. It is essential to cover the NucleoMag® Beads completely with elution buffer during the elution step. The volume of dispensed elution buffer depends on the magnetic separation system (e.g., the position of the pellet inside the separation plate). For efficient elution, the magnetic bead pellet should be resuspended completely in the elution buffer. For some separators, high elution volumes might be necessary to cover the whole pellet.

^{* 8-}channel pipetting device

3 Storage conditions and preparation of working solutions

Attention: Buffers MVL, MV2, and MV3 contain chaotropic salt! Wear gloves and goggles!

- All components of the NucleoMag[®] Virus kit should be stored at room temperature (18–25 °C) and are stable for up to one year.
- All buffers are delivered ready to use.

Lvsis Buffer MVL:

<u>Lysis Buffer MVL</u> may form salt precipitates upon storage. To re-dissolve the salt precipitate incubate the buffer bottle at 40 $^{\circ}$ C until all of the precipitate is re-dissolved.

<u>Lysis Buffer MVL with Carrier RNA</u>: Lysis Buffer MVL with added Carrier RNA can be stored at room temperature for 1–2 weeks.

Frequent warming, temperatures > 80 °C, and extended heat incubation will cause degradation of the Carrier RNA. This leads to reduced recovery of viral RNA and eventually false negative RT-PCR results, in particular, if low-titer samples are used. Do not warm Buffer MVL containing Carrier RNA more than 6 times!

Before starting any **NucleoMag® Virus** protocol, prepare the following:

- Proteinase K: Before first use of the kit, add 1.1 mL Proteinase Buffer PB to each vial of the lyophilized Proteinase K. Dissolved Proteinase K solution should be stored in aliquots at - 20 °C.
- Carrier RNA: Before first use of the kit, add 440 μL Carrier RNA Buffer to each vial lyophilized Carrier RNA. Store dissolved Carrier RNA solution in aliquots at - 20 °C.

	NucleoMag [®] Virus		
REF	1 x 96 preps 744800.1	4 x 96 preps 744800.4	
Proteinase K (lyophilized)	1 vial (20 mg) Add 1.1 mL Proteinase Buffer	4 vials (20 mg/vial) Add 1.1 mL Proteinase Buffer to each vial	
Carrier RNA (lyophilized)	1 vial (400 μg) Add 440 μL Carrier RNA Buffer	4 vials (400 μg/vial) Add 440 μL Carrier RNA Buffer to each vial	

4 Safety instructions

The following components of the **NucleoMag® Virus** kits contain hazardous contents.

Wear gloves and goggles and follow the safety instructions given in this section.

Only harmful features do not need to be labeled with H and P phrases up to 125 mL or 125 g.

Mindergefährliche Eigenschaften müssen bis 125 mL oder 125 g nicht mit H- und P-Sätzen gekennzeichnet werden.

Component	Hazard contents	GHS symbol	Hazard phrases	Precaution phrases
Inhalt	Gefahrstoff	GHS-Symbol	H-Sätze	P-Sätze
MVL	guanidine hydrochloride 50–66 % Guanidinhydrochlorid 50–66 % CAS 50-01-1	WARNING ACHTUNG	302, 315, 319	264, 280, 301+312, 302+352, 305+351+338, 330, 332+313, 337+313
MV2	sodium perchlorate 20–40 % and ethanol 35–55 % Natriumperchlorat 20–40 % und Ethanol 35–55 % CAS 7601-89-0 CAS 64-17-5	WARNING ACHTUNG	226, 302	210, 233, 301+312, 330, 370+378, 403+235
MV3	sodium perchlorate 5–20 % and ethanol 20–35 % Natriumperchlorat 5–20 % und Ethanol 20–35 % CAS 7601-89-0 CAS 64-17-5	WARNING ACHTUNG	226	210, 233, 370+378, 403+235
MV4	ethanol 55–75 % Ethanol 35–55 % CAS 64-17-5b	WARNING ACHTUNG	225	210, 233, 370+378, 403+235
Carrier RNA Buffer	guanidinium thiocyanate 30–60 % Guanidinthiocyanat 30–60 % CAS 593-84-0	WARNING ACHTUNG	302, 412, EUH031	260, 273, 301+312, 330
Proteinase K	proteinase K Proteinase K CAS 39450-01-6	DANGER GEFAHR	317, 334	261, 272, 280, 302+352, 304+340, 333+313, 342+311, 363

The symbol shown on labels refers to further safety information in this section.

Das auf Etiketten dargestellte Symbol weist auf weitere Sicherheitsinformationen dieses Kapitels hin.

Hazard phrases

Viral RNA/DNA isolation

H 225	Highly flammable liquid and vapour. Flüssigkeit und Dampf leicht entzündbar.
H 226	Flammable liquid and vapour. Flüssigkeit und Dampf entzündbar.
H 302	Harmful if swallowed. Gesundheitsschädlich bei Verschlucken.
H 315	Causes skin irritation. Verursacht Hautreizungen.
H 317	May cause an allergic skin reaction. Kann allergische Hautreaktionen verursachen.
H 319	Causes serious eye irritation. Verursacht schwere Augenreizung.
H 334	May cause allergy or asthma symptoms or breathing difficulties if inhaled. Kann bei Einatmen Allergie, asthmaartige Symptome oder Atembeschwerden verursachen.
H 412	Harmful in contact with skin. Schädlich für Wasserorganismen, mit langfristiger Wirkung.
EUH 031	Contact with acids liberates toxic gas. Entwickelt bei Berührung mit Säure giftige Gase.
Precaution p	hrases
P 210	Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking. Von Hitze, heissen Oberflächen, Funken, offenen Flammen sowie anderen Zündquellenarten fernhalten. Nicht rauchen.
P 233	Keep container tightly closed. Behälter dicht verschlossen halten.
P 260	Do not breathe dust/fume/gas/mist/vapours/spray. Staub/Rauch/Gas/Nebel/Dampf/Aerosol nicht einatmen.
P 261	Avoid breathing dust/fume/gas/mist/vapours/spray. Einatmen von Staub/Rauch/Gas/Nebel/Dampf/Aerosol vermeiden.
P 264	Wash thoroughly after handling. Nach Handhabung gründlich waschen.
P 272	Contaminated work clothing should not be allowed out of the workplace. Kontaminierte Arbeitskleidung nicht außerhalb des Arbeitsplatzes tragen.
P 273	Avoid release to the environment. Freisetzung in die Umwelt vermeiden.
P 280	Wear protective gloves/protective clothing/eye protection/face protection. Schutzhandschuhe/Schutzkleidung/Augenschutz/Gesichtsschutz tragen.
P 301+312	IF SWALLOWED: Call a POISON CENTER/doctor//if you feel unwell. BEI VERSCHLUCKEN: Bei Unwohlsein GIFTINFORMATIONSZENTRUM/Arzt/ anrufen.
P 302+352	
	IF ON SKIN: Wash with plenty of water / BEI BERÜHRUNG MIT DER HAUT: Mit viel Wasser / waschen.

Viral RNA/DNA isolation

P 305+351+338	IF IN EYES: Rinse cautiously with water for several minuts. Remove contact lenses, if present and easy to do. Continue rinsing. BEI KONTAKT MIT DEN AUGEN: Einige Minuten lang behutsam mit Wasser ausspülen. Eventuell vorhandene Kontaktlinsen nach Möglichkeit entfernen. Weiter ausspülen.
P 330	Rinse mouth. Mund ausspülen.
P 332+313	If skin irritation occurs: Get medical advice/attention. Bei Hautreizung: Ärztlichen Rat einholen/ärztliche Hilfe hinzuziehen.
P 333+313	If skin irritation or rash occurs: Get medical advice/attention. Bei Hautreizung oder -ausschlag: Ärztlichen Rat einholen/ärztliche Hilfe hinzuziehen.
P 337+313	If eye irritation persists: Get medical advice / attention. Bei anhaltender Augenreizung: Ärztlichen Rat einholen/ärztliche Hilfe hinzuziehen.
P 342+311	If experiencing respiratory symptoms: Call a POISON CENTER/doctor/ Bei Symptomen der Atemwege: GIFTINFORMATIONSZENTRUM/Arzt/ anrufen.
P 363	Wash contaminated clothing before reuse. Kontaminierte Kleidung vor erneutem Tragen waschen.
P 370+378	In case of fire: Use all extinguisher media to extinguish. Bei Brand: Alle Löschmittel zum Löschen verwenden.
P 403+235	Store in a well-ventilated place. Keep cool. An einem gut belüfteten Ort aufbewahren. Kühl halten.

5 Protocol for the isolation of viral RNA/DNA from cell-free body fluids

Protocol at a glance

- For hardware requirements refer to section 2.3.
- For detailed information on each step see page 16.

Before starting the preparation:

Check if Proteinase K and Carrier RNA were prepared according to section 3.

1	Lyse sample	10 μL Proteinase K 200 μL sample 4 μL Carrier RNA 200 μL MVL	
		Mix	
		56 °C, 10 min	
2	Bind viral RNA / DNA to NucleoMag [®] V-Beads	30 μL V-Beads 600 μL MV2	
		Mix by shaking for 5 min at RT (Optional: Mix by pipetting up and down)	↔
		Remove supernatant after 2 min separation	
3	Wash with MV3	Remove Square-well Block from NucleoMag [®] SEP 500 µL MV3	
		Resuspend: Shake 1 min at RT	↔
		Remove supernatant after 2 min separation	

4	Wash with MV4	Remove Square-well Block from NucleoMag [®] SEP	
		500 μL MV4	
		Resuspend: Shake 1 min at RT	↔
		Remove supernatant after 2 min separation	
5	Wash with MV5	550 μL MV5	
		Incubate for 45-60 s	
		Note: Do not resuspend the beads in Buffer MV5!	
		Remove supernatant	
6	Elute RNA/DNA	Remove Square-well Block from NucleoMag [®] SEP	
		50-100 μL MV6	
		Shake 5 min at 56 °C (Optional: Mix by pipetting up and down)	↔
		Separate 2 min and transfer viral RNA / DNA into elution plate / tubes	

Detailed protocol

This protocol is designed for magnetic separators with static pins (e.g., NucleoMag® SEP) and suitable plate shakers. It is recommended using a Square-well Block for separation (see section 6.2 ordering information). Alternatively, isolation of viral RNA/DNA can be performed in reaction tubes with suitable magnetic separators. This protocol is for manual use and serves as a guideline for adapting the kit to robotic instruments.

1 Lyse sample

Predispense 10 μ L Proteinase K and 200 μ L of sample to a suitable reaction tube. Add 200 μ L Buffer MVL (with added Carrier RNA) to the reaction tube (If Carrier RNA is not premixed with the Buffer MVL, add 4 μ L of the stock solution to the reaction tube). Mix well by repeated pipetting up and down and incubate at 56 °C for 10 min. Alternatively, lysis step can be performed in Tube Strips (see section 6.2 ordering information).

For higher convenience a premix of Proteinase K, Buffer MVL, and Carrier RNA can be prepared. This premix should be added to the sample immediately (within 15 min after preparation).

Following the lysis incubation, spin down to collect any sample from the lysis tube lids and transfer each lysate to the wells of a Square-well Block.

2 Bind viral RNA/DNA to magnetic beads

Add 30 µL resuspended V-Beads and 600 µL Buffer MV2 to the lysed sample.

Mix by pipetting up and down 6 times and **shake** for **5 min** at **room temperature**. Alternatively, when processing the kit without a shaker, pipette up and down 10 times and incubate for 5 min at room temperature.

NucleoMag® V-Beads and Buffer MV2 can be premixed.

Be sure to resuspend the NucleoMag[®] V-Beads before removing them from the storage bottle. Vortex storage bottle briefly until a homogenous suspension has been formed.

Separate the magnetic beads against the side of the wells by placing the Square-well Block on the NucleoMag[®] SEP a magnetic separator. Wait at least **2 min** until all the beads have been attracted to the magnets. Remove and discard supernatant by pipetting.

Do not disturb the attracted beads while aspirating the supernatant.

3 Wash with MV3

Remove the Square-well Block from the NucleoMag® SEP magnetic separator. Add **500 µL Buffer MV3** and resuspend the beads by shaking until the beads are resuspended completely (1–3 min). Alternatively, resuspend beads completely by repeated pipetting up and down.

Separate the magnetic beads by placing the Square-well Block on the NucleoMag® SEP magnetic separator. Wait at least 2 min until all the beads have been attracted to the magnet. Remove and discard supernatant by pipetting.

4 Wash with MV4

Remove the Square-well Block from the NucleoMag® SEP magnetic separator. Add **500 \muL Buffer MV4** and resuspend the beads by shaking until the beads are resuspended completely (1–3 min). Alternatively, resuspend beads completely by repeated pipetting up and down.

Separate the magnetic beads by placing the Square-well Block on the NucleoMag® SEP magnetic separator. Wait at least **2 min** until all the beads have been attracted to the magnet. Remove and discard supernatant by pipetting.

5 Wash with MV5

Leave the Square-well Block on the NucleoMag® SEP magnetic separator. Gently add 550 μ L Buffer MV5 to each well and incubate for 45–60 s while the beads are still attracted to magnets. Then aspirate and discard the supernatant.

Do not resuspend the beads in Buffer MV5. This step is to remove traces of ethanol and eliminates a drying step. Do not exceed incubation time of max. 1 min.

6 Elution

Add desired volume of **Buffer MV6** (50–100 μ L) to each well of the Square-well Block and resuspend the beads by shaking 5 min at 56 °C. Alternatively, resuspend beads completely by repeated pipetting up and down and incubate for 5 min at 56 °C.

Separate the magnetic beads by placing the Square-well Block on the NucleoMag® SEP magnetic separator. Wait at least **2 min** until all the beads have been attracted to the magnets. Transfer the supernatant containing the purified viral RNA/DNA to either microtubes or Tube Strips (see section 6.2 ordering information).

6 Appendix

6.1 Troubleshooting

Problem Po

Possible cause and suggestions

Insufficient elution buffer volume

Beads pellet must be covered completely with elution buffer.

Insufficient performance of elution buffer during elution step

Remove residual buffers during the separation steps completely.
 Remaining buffers decrease the efficiency of following wash and elution steps.

Poor yield/low sensitivity

Beads dried out

Do not let the beads dry as this might result in lower elution efficiencies.

Aspiration of attracted bead pellet

 Do not disturb the attracted beads while aspirating the supernatant, especially when the magnetic bead pellet is not visible in the lysate.

Aspiration and loss of beads

 Time for magnetic separation too short or aspiration speed too high.

Insufficient washing procedure

Low purity/low sensitivity

- Use only the appropriate combinations of separator and plate, for example, Square-well Block in combination with NucleoMag[®] SEP.
- Make sure that beads are resuspended completely during the washing procedure. If shaking is not sufficient to resuspend the beads completely mix by repeated pipetting up and down.

Carry-over of ethanol from wash buffers

Poor performance of RNA in downstream applications

- Be sure to remove all of the ethanolic wash solution Buffer MV4, as residual ethanol interferes with downstream applications. Ethanol evaporation from wash buffers
- Close buffer bottles tightly, avoid ethanol evaporation from buffer bottles as well as from buffer filled in reservoirs. Do not reuse buffers from buffer reservoirs.

Problem Possible cause and suggestions

Time for magnetic separation too short

Carry-over of beads

 Increase separation time to allow the beads to be completely attracted to the magnetic pins before aspirating any liquid from the well.

Aspiration speed too high (elution step)

 High aspiration speed during the elution step may cause bead carry-over. Reduce aspiration speed for elution step.

6.2 Ordering information

Product	REF	Pack of
NucleoMag [®] Virus	744800.1 744800.4	1 x 96 preps 4 x 96 preps
NucleoMag [®] SEP	744900	1
Square-well Blocks	740481 740481.24	4 24
Self adhering PE Foil	740676	50 sheets
Rack of Tube Strips (set consists of 1 Rack, 12 Tube Strips with 8 tubes each, and 12 Cap Strips)	740477 740477.24	4 sets 24 sets
KingFisher® Accessory Kit A (set consists of Square-well Blocks, Deep-well Tip Combs, Elution Plates for 4 x 96 NucleoMag® Virus preps using King Fisher® Flex platform)	744950	1 set
KingFisher® Duo Accessory Kit (set consists of KingFisher® Deep-well Blocks, KingFisher® Duo 12 Tip Combs, KingFisher® Duo Elution Strips for 8 x 12 NucleoMag® Virus preps using KingFisher® Duo / Duo Prime platform)	744952	1 set

Visit www.mn-net.com for more detailed product information.

6.3 Product use restriction/warranty

NucleoMag® Virus kit components are intended, developed, designed, and sold FOR RESEARCH PURPOSES ONLY, except, however, any other function of the product being expressly described in original MACHEREY-NAGEL product leaflets.

MACHEREY-NAGEL products are intended for GENERAL LABORATORY USE ONLY! MACHEREY-NAGEL products are suited for QUALIFIED PERSONNEL ONLY! MACHEREY-NAGEL products shall in any event only be used wearing adequate PROTECTIVE CLOTHING. For detailed information please refer to the respective Material Safety Data Sheet of the product! MACHEREY-NAGEL products shall exclusively be used in an ADEQUATE TEST ENVIRONMENT. MACHEREY-NAGEL does not assume any responsibility for damages due to improper application of our products in other fields of application. Application on the human body is STRICTLY FORBIDDEN. The respective user is liable for any and all damages resulting from such application.

DNA/RNA/PROTEIN purification products of MACHEREY-NAGEL are suitable for *IN VITRO*-USES ONLY!

ONLY MACHEREY-NAGEL products specially labeled as IVD are also suitable for *IN VITRO*-diagnostic use. Please pay attention to the package of the product. *IN VITRO*-diagnostic products are expressly marked as IVD on the packaging.

IF THERE IS NO IVD SIGN, THE PRODUCT SHALL NOT BE SUITABLE FOR *IN VITRO*-DIAGNOSTIC USE!

ALL OTHER PRODUCTS NOT LABELED AS IVD ARE NOT SUITED FOR ANY CLINICAL USE (INCLUDING, BUT NOT LIMITED TO DIAGNOSTIC, THERAPEUTIC AND/OR PROGNOSTIC USE).

No claim or representations is intended for its use to identify any specific organism or for clinical use (included, but not limited to diagnostic, prognostic, therapeutic, or blood banking). It is rather in the responsibility of the user or - in any case of resale of the products - in the responsibility of the reseller to inspect and assure the use of the DNA/RNA/protein purification products of MACHEREY-NAGEL for a well-defined and specific application.

MACHEREY-NAGEL shall only be responsible for the product specifications and the performance range of MN products according to the specifications of in-house quality control, product documentation and marketing material.

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There is no warranty for and MACHEREY-NAGEL is not liable for damages or defects arising in shipping and handling (transport insurance for customers excluded), or out of accident or improper or abnormal use of this product; defects in products or

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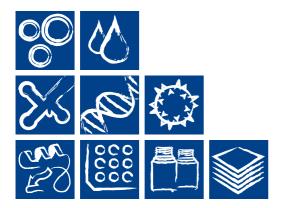
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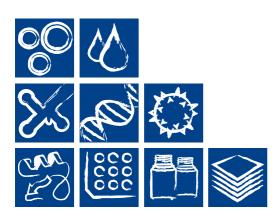
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