

INSTAND-EXTERNAL QUALITY ASSESSMENT SCHEMES MANUAL



INSTAND

Important notice

Different deadlines for return of results

Sample shipment: 02.09.2020

Deadline: 18.09.2020

Sample shipment: 16.09.2020

Deadline:

- for EQA groups 416 and 375 02.10.2020

- for EQA groups 349, 397, 399, 383 and 384 23.10.2020

Reporting of results for the following EQA schemes

Reporting of results for the following five EQA schemes should be done via the link independent from the INSTAND EQAS Online system:
<http://www.instand-ev.de/virus-resistance>

CMV resistance determination (349)

HBV resistance determination (397)

HCV resistance determination (399)

HIV-1 drug resistance determ. - standard progr. (383)

HIV-1 drug resistance determ. - additional progr. (384)

Instructions for Test Performance Virus Immunology and Virus Genome Detection September 2020

INSTAND reg. ass., Society for Research Promotion of Quality Assurance in Medical Laboratories reg. ass.

www.instand-ev.de

in collaboration with

Deutsche Vereinigung zur Bekämpfung der Viruskrankheiten e.V. (DVV)

Gesellschaft für Virologie e.V. (GfV)

Deutsche Gesellschaft für Hygiene und Mikrobiologie e.V. (DGHM)

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CONTENTS

General Information

Information on INSTAND External Quality Assessment (EQA) Schemes in Virus Diagnostics	4
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Virus Immunology

EQA Scheme <i>RiliBAEK parameters are marked according to the specified sections B2 and B3, respectively#</i>	No. of samples	Group	Page
Instructions for Virus Immunology			8
Chikungunya virus anti-CHIKV-IgG/IgM	4§	No. 402	10
Cytomegalovirus anti-CMV-IgG/IgM	2§	No. 351	10
Dengue Viruses anti-Dengue-IgG/IgM NS1 Ag	4§	No. 350	11
Please note the instruction for clinical interpretation on page 11			
Hantaviruses anti-Hanta-IgG/IgM	4§	No. 355	12
Hepatitis A Virus anti-HAV-IgG/IgM	4§	No. 343	13
Hepatitis B Virus (Prog. 1) HBsAg anti-HBs anti-HBc	12§	No. 344	13
Hepatitis B Virus (Prog. 2) anti-HBc-IgM HBeAg anti-HBe	6§	No. 345	14
Hepatitis C Virus anti-HCV HCV Ag	4§	No. 346	15
HIV-1/HIV-2 anti-HIV-1/2	4§	No. 335	15
HIV-1 p24 Antigen HIV-1 p24 Ag	2§	No. 337	16
SARS-CoV-2 anti-SARS-CoV-2 Please note the instruction for clinical interpretation on page 17 and 18	4§	No. 416	16
Rabies Virus anti-RABV	2§	No. 336	19
Zika Virus anti-ZIKV-IgG/IgM	3§	No. 338	19

§ You receive **1 tube** of each sample.

Unmarked EQA schemes are performed in conformity to the specified RiliBAEK Section B2 and B3, resp.

Virus Genome Detection

EQA Scheme <i>RiliBAEK parameters are marked according to the specified section B3#</i>	No. of samples	Group	Page
Instructions for Virus Genome Detection			20
BK Virus BK Virus DNA	4*	No. 364	23
Chikungunya Virus CHIKV RNA	4*	No. 392	23
Cytomegalovirus CMV DNA	4* <i>RiliBAEK B 3</i>	No. 365	24
CMV resistance determination CMV resistance	4*	No. 349	24
Dengue Viruses DENV RNA	4*	No. 369	25
Hepatitis A Virus HAV RNA	4* <i>RiliBAEK B 3</i>	No. 377	26
Hepatitis B Virus HBV DNA	4* <i>RiliBAEK B 3</i>	No. 361	26
HBV resistance determination HBV resistance	4*	No. 397	27
Hepatitis C Virus HCV-RNA	4* <i>RiliBAEK B 3</i>	No. 362	28
HCV Genotyping/Subtyping HCV Genotype/Subtype	5§ <i>RiliBAEK B 3</i>	No. 375	28
Please note the information on subtype differentiation for samples positive for HCV genotype 1.			
HCV resistance determination HCV resistance	4§	No. 399	29
Hepatitis D Virus HDV RNA	4*	No. 400	30
Hepatitis E Virus HEV-RNA	4* <i>RiliBAEK B 3 (as of RiliBAEK 2019)</i>	No. 380	31
HIV-1 (RNA) HIV-1 RNA	4* <i>RiliBAEK B 3</i>	No. 360	31
HIV-1 drug resistance determ. <i>standard program for protease inhibitors and reverse transcriptase inhibitors</i> HIV-1 drug resistance	4*	No. 383	32
HIV-1 drug resistance determ. <i>Additional program for integrase inhibitors and determination of tropism</i> HIV-1 drug resistance	2*	No. 384	33
Human herpesvirus 6 (HHV-6) HHV-6 DNA	4*	No. 405	35
JC Virus JC Virus DNA	4*	No. 394	36
Parainfluenza Viruses PIV RNA	4*	No. 388	36
Parechovirus HPeV RNA	4*	No. 407	37
Parvovirus B19 Parvo B19 DNA	4* <i>RiliBAEK B 3</i>	No. 367	37

§ You receive **1 tube** of each sample.

* You receive **2 tubes** of each sample.

Unmarked EQA schemes are performed in conformity to the specified RiliBAEK Section B2 and B3, resp.

Virus Genome Detection (continued)

EQA Scheme <i>RiliBAEK parameters are marked according to the specified section B3[#]</i>	No. of samples	Group	Page
Rabies Virus RABV RNA	4*	No. 390	38
Torque Teno Virus TTV-DNA NEW	4*	No. 408	38
West Nile Virus WNV RNA <i>RiliBAEK B 3 (as of RiliBAEK 2019)</i>	6*	No. 391	39
Zika Virus ZIKV RNA	4*	No. 403	39

§ You receive **1 tube** of each sample.

* You receive **2 tubes** of each sample.

Unmarked EQA schemes are performed in conformity to the specified RiliBAEK Section B2 and B3, resp.

INSTAND Expert Laboratories

INSTAND Expert Laboratories for EQASs in Virus Diagnostics	Page 40
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Return of results

Different deadlines for return of results

Sample shipment: 02.09.2020

Deadline: 18.09.2020

Sample shipment: 16.09.2020

Deadline:

- for EQA groups

416 and 375 **02.10.2020**

- for EQA groups

349, 397, 399, 383 and 384 **23.10.2020**

EQAS Online system - result entry

Please enter your results in the INSTAND EQAS Online system using the link:

www.instand-ev.de/en.html -> "EQAS Online" ->

"Ordering online and entering results".

In case of questions regarding the EQAS Online system, please contact INSTAND e.V.:

Tel.: +49-(0)211-15 92 13 0

Email: support@instand-ev.de

Electronic reporting of results for EQA schemes for virus resistance determination

Separate instructions for EQA schemes for virus resistance determination:

349, 383, 384, 397 and 399

Extended deadline: **23.10.2020**

For electronic reporting of the results please see the specific information for test performance of the respective EQA scheme and the link:

<http://www.instand-ev.de/virus-resistance>

Information on INSTAND EQA Schemes in Virus Diagnostics

General instruction for the use of INSTAND EQAS samples

- INSTAND EQA samples must only be used for in vitro diagnostic purpose following the "information for test performance" in this INSTAND manual and – in case of apparent test-immanent problems of certain in vitro diagnostic medical devices (IVDs) – for inspection of the relevant IVD.
- INSTAND EQA samples must not be misused for recombinant production of pathogens or pathogen moieties, neither for scientific nor commercial use.
- EQA scheme samples should not be diluted or mixed.
- The samples must not be used for therapeutic or prophylactic applications.
- The samples must not be handed over to other parties without agreement of INSTAND e.V. and must not be used for other external quality assessment schemes without agreement of INSTAND e.V.

Precautions

- All samples must be considered and treated as potentially infectious materials.
- All relevant regulations and legal conditions for handling of infectious materials and performance of direct and/or indirect detection of infectious pathogens.

1 INSTAND EQA schemes in virus diagnostics and RiliBAEK

1.1 Requirements specified in the RiliBAEK

The Guidelines of the German Medical Association (RiliBAEK) specifies the basic principles of internal and external quality assurance of all laboratory medical analyses including those in virus diagnostics.

Please note:

According to the decision of the Executive Board of the German Medical Association from 18 October 2019, a new guideline on quality assurance (RiliBAEK) of the German Medical Association has been released on 23 December 2019 in the "Deutsches Ärzteblatt" (www.bundesaerztekammer.de/rilibaek2019) (DOI: 10.3238/arztebl.2019.rili_baek_QS_Labor20192312). An English version will follow.

With regard to the EQA schemes in virus diagnostics, the following analyses were included as new analyses which are subject to the RiliBAEK:

Immunological EQA schemes stated in Table B 2-2

- measles virus, antibodies against
- mumps virus, antibodies against
- varicella zoster virus, antibodies against

EQA schemes for the direct detection of infectious agents stated in Table B 3-2

- hepatitis E virus, genome detection
- measles virus, genome detection
- mumps virus, genome detection
- norovirus, genome detection
- rubella virus, genome detection
- West Nile virus, genome detection

The previous RiliBÄK version in accordance with the decision of the Executive Board from 11 April 2014 and 20 June 2014 (published in German language: Deutsches Ärzteblatt, Jg. 111, Heft 38, 19.

November/December 2014, A 1583 - A 1618; https://www.bundesaerztekammer.de/fileadmin/user_upload/downloads/pdf-Ordner/RL/Rili-BAEK-Laboratoriumsmedizin.pdf) will expire on 22 December 2021 after the end of the transition period. For an English translation of this previous version please see: Guidelines of the German Medical Association on quality assurance in medical laboratory testing. GMS Z Forder Qualitätssich Med Lab. 2015;6:Doc03. DOI: 10.3205/lab000018, URN: urn:nbn:de:0183-lab0000182. <http://www.egms.de/static/pdf/journals/lab/2015-6/lab000018.pdf>

All qualitative and quantitative analyses in virus diagnostics are subject to internal quality assurance.

All analyses in virus diagnostics which are specified for external quality assurance in the corresponding tables of the different RiliBAEK sections are subject to mandatory participation in the corresponding EQA schemes.

Please note that also the analyses of those parameters which are not yet stated in the specified section B 2 (Table B 2-2) and specified section B 3 (Table B 3-2) are nevertheless subject to external quality assurance. The corresponding EQA schemes will be organized by INSTAND in compliance to the RiliBAEK.

1.2 Specified RiliBAEK section B 2 "Qualitative medical laboratory testing"

The quality assurance of all tests for the detection of virus specific antibodies has been assigned to Section B 2 of the RiliBAEK "qualitative medical laboratory testing".

Reporting a result of a test for virus specific antibody detection primarily qualitatively as "positive", "negative" or "borderline/indeterminate" implies that the quality assurance of the corresponding test has to be performed according to RiliBAEK section B 2 (qualitative medical laboratory testing). In this case, quantitative statements on antibody concentrations (i.e. as units/volume) can additionally be reported in brackets for orientation. Please note that primary reporting of antibody concentration alone or in front of the qualitative result directly implies that the quality assurance of the corresponding test has to be performed according to RiliBAEK section B 1 ("quantitative medical laboratory testing").

Please note that determination of titers is considered as qualitative analysis (see section A of RiliBAEK "Basic requirements for quality assurance in medical laboratory testing").

1.3 Specified RiliBAEK section B 3 "Direct detection and characterisation of infectious agents"

Please note the requirements in regard to the evaluation of the results for the quantitative virus genome detection of CMV, HBV, HCV and HIV-1 (RNA).

These requirements for the "acceptable deviation of a quantitative result expressed as log 10 value measured by an individual laboratory in respect to the target value expressed as log 10 value obtained in the EQA scheme by the participating laboratories" have been amended. The requirements are defined in Table B 3-2a "External quality assurance for the detection of concentration of nucleic acids of CMV, HBV, HCV and HIV-1 (RNA) in blood/plasma/serum" = "Externe Qualitätssicherung bei der Bestimmung der Nukleinsäurekonzentration in Blut/Plasma/Serum" (see Table A / column 3).

Table A
External quality assurance for the detection of concentration of nucleic acids of CMV, HBV, HCV and HIV-1 (RNA) in blood/plasma/serum

(see Table B 3-2a in: Deutsches Ärzteblatt, Jg. 110; Heft 12, 22. März 2013, A 575-582)

1 No.	2 Analyte	3 Acceptable deviation of a quantitative result expressed as log ₁₀ value measured by an individual laboratory in respect to the target value expressed as log ₁₀ value obtained in the EQA scheme by the participating laboratories	4 Range of validity in respect to column 3			5 Target value obtained in the EQA scheme	6 Frequency of the EQA scheme
			from	to	measurement unit		
1	CMV DNA	-0,8 to +0,8	5 000	5 mio	IU/mL	SW*	half-year
2	HBV DNA	-0,6 to +0,6	500	5 mio	IU/mL	SW*	half-year
3	HCV RNA	-0,6 to +0,6	500	5 mio	IU/mL	SW*	half-year
4	HIV-1 RNA	-0,6 to +0,6	500	5 mio	copies/mL	SW*	half-year

* SW = Sollwert = target value: The target value is defined as arithmetic mean value or median value (if applicable) of the results obtained in an EQA scheme

Please note for the analytes stated in Table A/ column 2:

Evaluation of results for quantitative genome detection of CMV

Notice for German and foreign participants of EQA scheme 365:

For evaluation, "IU/ml" have primarily been considered as measurement units of the quantitative results for the analyte CMV. This is in accordance to the "Guidelines of the German Medical Association (Bundesärztekammer / RiliBÄK)", Specified RiliBÄK Section B 3, Table B. 3-2a,

When applying CE-marked tests, which not (yet) allow reporting of results in IU/mL, it should be continued to report the results as stated by the manufacturer.

Evaluation of results for quantitative genome detection of HBV and HCV

Notice for German participants of EQA schemes 361 and 362:

For evaluation, "IU/ml" have been considered as measurement units of the quantitative results for the analytes HBV and HCV. This is in accordance to the "Guidelines of the German Medical Association (Bundesärztekammer / RiliBÄK)", Specified RiliBÄK Section B 3, Table B. 3-2a.

Statements in "copies/ml" will not be accepted anymore.

Notice for foreign participants of EQA schemes 361 and 362:

Please note that quantitative results in "copies/ml" for the genome detection of HBV and HCV, respectively, have not been evaluated due to the low number of analyses.

Evaluation of results for quantitative genome detection of HIV-1 (RNA)

Notice for German participants of EQA scheme 360:

For evaluation, "copies/ml" have been considered as measurement unit of the quantitative results for the analyte HIV-1 (RNA). This is in accordance to the "Guidelines of the German Medical Association (Bundesärztekammer / RiliBÄK)", Specified RiliBÄK Section B 3, Table B. 3-2a.

Statements in "IU/ml" will not be accepted anymore.

Notice for foreign participants of EQA scheme 360:

Please note that quantitative results in "IU/ml" for the genome detection of HIV-1 (RNA) have not been evaluated due to the low number of analyses.

1.4 Validity period of certificates of the INSTAND EQA schemes in virus diagnostics

The RiliBAEK defines the validity period of a certificate of successful participation for each of the EQA schemes stated in Table B 2-2 and Table B 3-2 (external quality assurance = Externe Qualitätssicherung/Ringversuche) as twice as long as the frequency for mandatory participation.

Please note that also the analyses of those parameters which are not yet stated in both tables are nevertheless subject to external quality assurance. The corresponding EQA schemes will be organized by INSTAND in compliance to the RiliBAEK.

This means that the validity period of the certificates of successful participation for most of the INSTAND EQA schemes in virus diagnostics will be one year.

This concerns the EQA schemes in virus diagnostics performed with a frequency of four times per year (Table B) as well as those schemes performed twice a year (Table C). The validity period of certificate will be two years for EQA schemes performed once a year.

The validity period of the certificate of the "Special EQA program in accordance with the RKI-entero surveillance program - Virus Detection - Enterovirus-PCR / cultivation and typing" (program 374) will be agreed with the National Reference Center for Poliomyelitis and Enteroviruses, Regional Reference Laboratory of WHO/EURO for Poliomyelitis, Robert Koch-Institute, Berlin.

1.5 Evaluation criteria for the results of a defined EQA scheme in virus diagnostics

The certificate of successful participation of a defined EQA scheme in virus diagnostics is assigned to a defined parameter. Each parameter is individually evaluated in the certificate of successful participation and listed in all participation and evaluation documents.

The evaluation criteria for the results of EQA schemes for the detection of virus specific antibodies follow the Guideline of the German Medical Association, RiliBAEK section E 2 (specific requirements on EQA schemes for qualitative laboratory medical analyses = Spezielle Anforderungen an Ringversuche bei qualitativen laboratoriumsmedizinischen Untersuchungen). For receiving a certificate of successful participation for a defined EQA scheme it is required that you analyzed all samples of the sample set correctly with the same method in the corresponding parameter (100% correct results according to the target values).

Please note: A corresponding proceeding is applied in section E 3 (specific requirements on EQA schemes for direct detection and characterization of infectious pathogens = Spezielle Anforderungen an Ringversuche zum laboratoriumsmed. Nachweis und zur Charakterisierung von Infektionserregern) for tests for virus antigen and genome detection. Specifications will follow.

2 Provision of participation documents of a defined EQA scheme term (certificate, certificate of participation and listing and evaluation of results) and summary of sample properties and target values

Since the EQA term **September 2019**, *participation documents* (certificate, certificate of participation and listing and evaluation of results) of the INSTAND EQA schemes in virus diagnostics will be available only in the "EQAS (RV) Online system" (<https://rv-online.instandev.de/index.shtml?lang=en>) when the evaluation will have been completed (Tables B and C).

The *summary of sample properties and target values* is available:

- by email with a link to the document "Summary of sample properties and target values" and
- on the INSTAND homepage under "EQAS Online / Service for EQA tests / EQA area (Virus immunology / Virus genome detection)" in English language: <http://www.instand-ev.de/en/eqas-online/service-for-eqa-tests.html> and in German language: <http://www.instand-ev.de/ringversuche-online/ringversuche-service.html>.

Table B: EQA schemes – performed with a frequency of four times per year
<i>Virus immunology:</i> Cytomegalovirus (351) Hepatitis A virus (343) Hepatitis B virus Prog. 1 (344) Hepatitis B virus Prog. 2 (345) Hepatitis C virus (346) HIV-1/HIV-2 (335) HIV-1 p24 Ag (337)
<i>Virus genome detection:</i> Cytomegalovirus (365) Hepatitis A virus (377) Hepatitis B virus (361) Hepatitis C virus (362) Hepatitis E virus (380) HIV-1 (RNA) (360) Parvovirus B19 (367) West Nile virus (391)

Table C: EQA schemes – performed twice per year or with lower frequency
<i>Virus immunology:</i> Borna disease viruses (415) Chikungunya virus (402) Dengue viruses (Ab/NS1-Ag) (350) Epstein Barr virus (352) TBE (FSME) virus (358) Hantaviruses (355) Hepatitis D virus (347) Hepatitis E virus (348) Herpes simplex viruses (354) HTLV-1/HTLV-2 (339) Measles virus (357) Mumps virus (356) Parvovirus B19 (342) Rubella virus (341) Rabies (Tollwut) virus (336) SARS-CoV-2 (416) Varicella zoster virus (353) Zika virus (338)


Table C (continued): EQA schemes – performed twice per year or with lower frequency
<i>Virus genome detection:</i> Adenoviruses (371) BK virus (364) Borna disease viruses (404) Chikungunya virus (392) Coronaviruses incl. SARS-CoV-2 (340) Cytomegalovirus training program (368) Cytomegalovirus resistance determination (349) Dengue viruses (369) Enteroviruses (372) RKI-Entero-Surveillance (every two years) (374) Epstein Barr virus (376) Gastrointestinal Virus Panel for Multiplex Tests (430) Hepatitis B virus training program (378) Hepatitis B virus genotyping (396) Hepatitis B virus resistance determination (397) Hepatitis C virus training program (379) Hepatitis C virus geno-/subtyping (375) Hepatitis C virus resistance determination (399) Hepatitis D virus (400) Herpes simplex virus type 1/2 (363) HIV-1 (RNA) training program (382) HIV-1 drug resistance determ. (standard progr.) (383) HIV-1 drug resistance determ. (additional progr.) (384) HIV-2 (RNA) (395) Human herpesvirus 6 (HHV-6) (405) Human herpesvirus 8 (HHV-8) (406) Human Metapneumovirus (385) Human Papilloma viruses (373) Human Rhinoviruses (393) <i>Influenza viruses (genome/Ag) (370)&</i> JC virus (394) Measles virus (386) Mumps virus (387) <i>Norovirus (381)&</i> Parainfluenza viruses (388) Parechovirus (407) Panel for viral meningitis/encephalitis f. multiplex tests (433) Respiratory Virus Panel 1 for Multiplex Tests (431) Respiratory Virus Panel 2 for Multiplex Tests (432) Respiratory syncytial virus (Ag/genome) (359) Rotaviruses (401) Rubella virus (389) Rabies (Tollwut) virus (390) Torque teno virus (TTV) (408) Varicella zoster virus (366) Zika virus (403)

[&] The two terms of the EQA schemes "Influenza viruses" (370) and "Norovirus" (381), respectively, have been appointed to the winter season, i.e. November and March of the following year. The provision of participation documents (certificates of successful participation, statements of participation and statements of individual results) of the November term follows the specifications as described for the EQA schemes in Table B.

3 Electronic supply of summary and reports of the EQA schemes in virus diagnostics

You will be informed by email when the electronic version of the summary of the respective EQA scheme is available on the INSTAND homepage.

Regarding the reports of the individual EQA schemes the email on the electronic availability is sent out in due time before the next run of the corresponding EQA schemes. This email includes a table allowing you to directly open and/or save the documents by clicking the respective download button/s. An example is:

Virus immunology EQA schemes June 2017		
335	HIV-1 / HIV-2	

INSTAND urgently needs your email address for the purpose of electronic supply of the summary and reports.

4 Release of reports of EQA schemes in virus diagnostics on the INSTAND homepage

Each report of a defined EQA scheme will be released on the INSTAND homepage immediately after completion. The reports as well as the summary of this EQA scheme are available as PDF file on the INSTAND-homepage under EQAS Online / Service for EQA tests / EQA area (Virus Genome Detection) in English language (<http://www.instand-ev.de/en/eqas-online/service-for-ega-tests.html>).

VIRUS IMMUNOLOGY

Instructions for Virus Immunology

1. Storage of samples

The samples should be stored in a refrigerator (+2°C to +8°C) directly after receipt.

2. Pre-treatment of the serological samples

All samples of the EQA programs in virus immunology 335-358 consist of sera or plasmas, which were frozen after preparation and were allowed to thaw during transport. Although only sera or plasmas with supreme quality were selected for sample preparation, lipid aggregates may form after thawing and float in some of the samples.

IMPORTANT INSTRUCTION!

Please note: Prior to testing all samples have to be stored in a refrigerator (+2°C to +8°C) in an upright position (test tube rack). In order to separate possible lipid aggregates it is recommended to **centrifuge** the samples in their original tubes **preferentially at 10,000 RCF** (Relative Centrifugal Force) for **10 min between +4°C and +8°C** (e.g., in a refrigerated Eppendorf centrifuge). At least standard centrifugation conditions for serum preparation (for removing the clot) should be applied. In case a refrigerated centrifuge is not available, the original sample tubes should be kept refrigerated before and after the centrifugation step.

In case a **lipid layer** has been formed after centrifugation on top of serum/plasma, please carefully take out the serum/plasma below the lipid layer. A second centrifugation step in the cold may be required. After the centrifugation step the serum/plasma can be used for further testing under standard conditions.

In case of application of **MEIAs** please follow the manufacturer's instructions.

In case of **rapid tests for anti-HIV** the centrifugation step can be dispensed (please see the instructions for EQA programs 335 and 337).

3. Test performance

See following instructions for test performance for the corresponding EQA program.

4. Reporting of results

4.1 RiliBAEK section B 2 states that reporting a result of a test for virus specific antibody detection primarily qualitatively as "positive", "negative" or "borderline/indeterminate". A statement of titer or antibody concentration (units per volume) can additionally be reported in brackets for orientation. Please see the homepage of the German Medical Association for FAQs / "Häufig gestellte Fragen zur Richtlinie der Bundesärztekammer zur Qualitätssicherung laboratoriumsmedizinischer Untersuchungen" (http://www.bundesaerztekammer.de/fileadmin/user_upload/downloads/pdf-Ordner/QS/FAQ-Rili-BAEK.pdf).

4.2 **Qualitative results** should be stated as "reactive"/"positive", "non-reactive"/"negative" or "borderline"/"indeterminate".

4.3 For statements of titers and concentrations (e.g. IU/l, U/ml, pg/ml etc.) please note:

- **Positive samples:** Please report the actual antibody concentration you have determined.
- **Negative samples:** Only for the titer of antibody negative samples the reporting of the lowest dilution step (e.g. < 1:X) will be accepted.
- Statements of titers and concentrations **have to be reported together** with the qualitative result. Please note for samples positive for anti-rubella that the result of hemagglutination inhibition tests should exclusively stated as titer.

4.4 Please note that we ask you to report also the **raw data of your analyses** (e.g. s/co, index etc.). We will start to show these raw data in the final reports in due time.

4.5 The simultaneous reporting of different results for one test will be evaluated as a failure.

Example: EQAS for HIV-1

Anti-HIV-1/HIV-2 ELISA of manufacturer X:

The **simultaneous reporting** of a "positive" and "borderline" result is not accepted.

4.6 In order to get a comprehensive evaluation of all tests performed in the different laboratories it is necessary to collect as many results as possible. In case you receive deviating results for a given sample by applying tests from different manufacturers, please indicate which of the results should be considered for your certificate.

Example: EQAS for HIV-1

Anti-HIV-1/HIV-2 ELISA of manufacturer X:

Result "positive";

Anti-HIV-1/HIV-2 ELISA of manufacturer Y:

Result "negative".

You should indicate that **only the result** from the analysis performed with the ELISA of the manufacturer X **should be considered**.

4.7 All samples of a sample set (also negative samples) have to be analyzed with all methods routinely used in your laboratory [please note the special recommendation for confirmation testing of HBsAg-negative samples; see program hepatitis B1 (344)]. Please keep in mind that only this strategy will allow the detection of **problems of sensitivity and specificity** for the different tests and methods. In case you get discrepant results by this approach, you can indicate this observation without any disadvantages for your certificate.

4.8 Results of **avidity determinations** can be reported for the following EQA programs:

- 338 Zika virus
- 341 rubella virus
- 342 parvovirus B19
- 351 cytomegalovirus
- 352 Epstein Barr virus
- 353 varicella zoster virus
- 354 herpes simplex viruses
- 356 mumps virus
- 357 measles virus
- 358 TBE (FSME) virus
- 402 Chikungunya virus
- 416 SARS-CoV-2

5. Acceptance of results of complement fixation tests (CFTs) for INSTAND EQA programs and accreditation of virus diagnostic laboratories

The previous INSTAND EQA programs in virus immunology documented a lower sensitivity of CFT in comparison to other modern methods for the detection of virus specific antibodies. The CFT regularly revealed false negative results. The Diagnostic Council of the German Association for the Control of Virus Diseases (Deutsche Vereinigung zur Bekämpfung der Viruskrankheiten, DVV) and the German Society for Virology (Gesellschaft für Virologie, GfV) has therefore decided that **CFT is no longer recommended as state-of-the-art method for the detection of antibodies against measles, mumps, rubella, tick borne encephalitis as well as polio-, coxsackie-, echo- and other enteroviruses.**

Since 2007 results obtained by CFT for the detection of above-mentioned virus specific antibodies will not be accepted anymore for the INSTAND certificates. In case you will report CFT results, these data will only be documented in the EQA program reports.

Please see (only in German language):

"Beschlüsse des Sektorkomitees Medizinische Laboratorien zu Anforderungen der DIN EN ISO 15189:2014 an die Qualität und Kompetenz von Medizinischen Laboratorien", Beschluss 5.5-06 "Virusdiagnostische Tests: Komplementbindungsreaktion (KBR) zum Nachweis virusspezifischer Antikörper"

https://www.dakks.de/sites/default/files/dokumente/7_1_sd_3_025_beschluesse_sk_medlab_20171117_v1.4.pdf

Virus Immunology Chikungunya virus (402)

anti-CHIKV-IgG/IgM

conform to RiliBAEK B 2

September 2020

Virus Immunology Cytomegalovirus (351)

anti-CMV-IgG/IgM

conform to RiliBAEK B 2

September 2020

Instructions for test performance

Samples 402018, 402019, 402020, 402021
sera (0.3 ml each)

Precautions

The sera are negative for HIV, HBV and HCV (by serology). The samples are not heat inactivated and must be considered and treated as potentially infectious material. RNA positive samples are heat inactivated (60 min at 65°C). All sera must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples should be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

Please note the "**Instructions for Virus Immunology**". The samples are non-lyophilized sera and plasma samples (0.3 ml each) and should be **centrifuged preferentially at 10,000 RCF** (Relative Centrifugal Force) for **10 min between +4°C and +8°C**. At least standard centrifugation conditions for serum preparation (for removing the clot) should be applied.

Test performance and result entry to EQAS Online (= "RV-Online") system

The samples should be analyzed for IgG and IgM antibodies against chikungunya virus (anti-CHIKV-IgG/anti-CMV-IgM) or for total antibodies against chikungunya virus (anti-CHIKV-total) applying all tests routinely used in your laboratory (even for a negative sample).

Parameter (formerly: test category):

- "Anti-CHIKV IgG"
- "Anti-CHIKV IgG - avidity"
- "Anti-CHIKV IgM"

All results should be reported according to the requests of the entry mask in EQAS Online.

Titers, concentrations (Units/volume) as well as **raw data of your analyses** as S/CO, Index etc. should be reported separately. We will start to show these raw data in the final reports in due time.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

For guidance of result entry, see page 3 and Annex 1.

Deadline: 18.09.2020

Instructions for test performance

Samples 351083, 351084
sera (0.5 ml each)

Precautions

The sera are negative for HIV, HBV and HCV (by serology). The samples are not heat inactivated and must be considered and treated as potentially infectious. Samples positive for virus specific IgM are potentially infectious for the corresponding virus. All sera must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples should be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

Please note the "**Instructions for Virus Immunology**". The samples are non-lyophilized sera (0.5 ml each) and should be **centrifuged preferentially at 10,000 RCF** (Relative Centrifugal Force) for **10 min between +4°C and +8°C**. At least standard centrifugation conditions for serum preparation (for removing the clot) should be applied.

Test performance and result entry to EQAS Online (= "RV-Online") system

The samples should be analyzed for IgG and IgM antibodies against cytomegalovirus (anti-CMV-IgG/anti-CMV-IgM) or for total antibodies against cytomegalovirus (anti-CMV-total) applying tests routinely used in your laboratory (even for a negative sample).

Parameter:

- "Anti-CMV IgG"
- "Anti-CMV IgG - avidity"
- "Anti-CMV IgM"

All results should be reported according to the requests of the entry mask in EQAS Online.

Titers, concentrations (Units/volume) as well as **raw data of your analyses** as S/CO, Index etc. should be reported separately. We will start to show these raw data in the final reports in due time.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: 18.09.2020

Virus Immunology Dengue Viruses (350)

anti-Dengue-IgG/IgM
NS1 antigen

conform to RiliBÄK B 2
conform to RiliBÄK B 3

September 2020

Instructions for test performance

Samples **350082, 350083, 350084, 350085**
sera (0.3 ml each)

Precautions

The sera are negative for HIV, HBV and HCV (by serology). The samples are not heat inactivated and must be considered and treated as potentially infectious material. NS1 antigen positive samples as well as RNA positive samples are heat inactivated (60 min at 65°C). All sera must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples should be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

Please note the "Instructions for Virus Immunology". The samples are non-lyophilized sera (0.3 ml each) and should be **centrifuged at least at 10,000 RCF** (Relative Centrifugal Force) for **10 min between +4°C and +8°C**.

Test performance and result entry to EQAS Online (= "RV-Online") system

The samples should be analyzed for IgG and IgM antibodies against dengue viruses (anti-dengue-IgG and anti-dengue-IgM, respectively) as well as for dengue virus antigen NS1 applying all tests routinely used in your laboratory. **All samples** (even a negative sample) should be analyzed applying the **same tests**.

Parameter:

- "Anti-dengue virus IgG"
- "Anti-dengue virus IgM"
- "Dengue virus-NS1 Ag"
- "Clinical interpretation"

All results should be reported according to the requests of the entry mask in EQAS Online.

Titers, concentrations (Units/volume) as well as **raw data of your analyses** as S/CO, Index etc. should be reported separately. We will start to show these raw data in the final reports in due time.

Clinical interpretation of the tested samples

Please differentiate, if the corresponding sample's immunological parameters are typical for:

- an acute infection

(immunological parameters are:

NS1-Ag pos., anti-Dengue-IgG neg., anti-Dengue-IgM neg.
or

NS1-Ag pos., anti-Dengue-IgG neg., anti-Dengue-IgM pos.
or

NS1-Ag pos., anti-Dengue-IgG pos., anti-Dengue-IgM pos.)

- a recent infection

(immunological parameters are:

NS1-Ag neg., anti-Dengue-IgG pos., anti-Dengue-IgM pos.)

- a past infection

(immunological parameters are:

NS1-Ag neg., anti-Dengue-IgG pos., anti-Dengue-IgM neg.)

- a negative status of infection

(immunological parameters are:

NS1-Ag neg., anti-Dengue-IgG neg., anti-Dengue-IgM neg.)

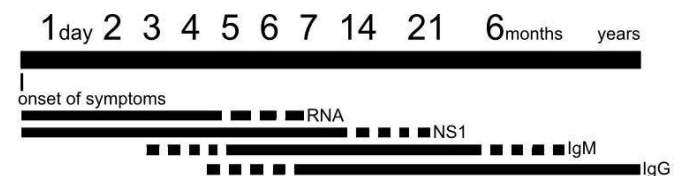
Please note:

A statement on an **acute dengue virus infection must be based on the presence of NS1 antigen** detected by a reliable test. Applying only tests for the detection of anti-dengue-IgG and anti-dengue-IgM without testing on NS1 antigen does not allow a statement on an acute dengue virus infection.

PLEASE NOTE

and consider figure 1 with the course of the diagnostic parameters of a primary dengue virus infection for the clinical interpretation.

Figure 1: Diagnostic parameters of a primary dengue virus infection (Schmidt-Chanasit)



Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline:

18.09.2020

Virus Immunology Hantaviruses (355)
anti-Hanta-IgG/IgM conform to RiliBÄK B 2
September 2020

Instructions for test performance

Samples 355081, 355082, 355083, 355084
sera (0.5 ml each)

Precautions

The sera are negative for HIV, HBV, and HCV (by serology) and **negative for hantavirus RNA**. The samples are not heat inactivated. All sera must be considered and treated as potentially infectious material and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples should be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Diagnostic problem and anamnestic information

The 4 samples can comprise sera from:

- patients with an acute hantavirus infection (characteristic symptoms such as elevated creatinine, flu-like symptoms and abnormal fatigue);
- patients with a past hantavirus infection;
- blood donors without any indication of a hantavirus infection.

An anamnesis concerning a stay abroad outside Europe is not known. Detailed anamnestic data will be available in the final evaluation of this EQA scheme.

Final evaluation and criteria for passing this EQA scheme successfully

This EQA scheme will place main emphasis on the final evaluation of the infection status for each of the samples.

Prerequisite for passing this EQA scheme successfully will be your statement for:

Parameter 98:

Status of hantavirus infection (without differentiation of serotype)

Please state your result for the status of hantavirus infection without further differentiation of serotype specific antibodies and report for each sample if it represents

- evidence for an acute infection,
- evidence for a past infection or
- no evidence for infection.

Additionally, results will be considered for:

Parameter 99:

Serotype differentiation (only accepted together with infection status)

Please extend your final statement of the status of infection for each sample with the causative hantavirus serotype and consider the **anamnestic information**.

ATTENTION:

Your statement in parameter 99 is **only accepted together with your status of infection** in parameter 98. **Statements of more than one serotype will be considered as "incorrect"**.

Pre-treatment of the samples

Please note the "**Instructions for Virus Immunology**". The samples are non-lyophilized sera (0.5 ml each) and should be **centrifuged at least at 10,000 RCF** (Relative Centrifugal Force) for **10 min between +4°C and +8°C**.

Test performance and result entry to EQAS Online (= "RV-Online") system

The samples should be analyzed for IgG and IgM antibodies against hantaviruses (anti-hantavirus-IgG/anti-hantavirus-IgM) applying all tests routinely used in your laboratory (even for a negative sample).

Parameter:

- "Anti-hantavirus IgG - ELISA / IFT / Rapid Test"
- "Anti-hantavirus IgM - ELISA / IFT / Rapid Test"
- "Anti-hantavirus IgG - Immunoblot"
- "Anti-hantavirus IgM - Immunoblot"
- "Anti-hantavirus IgG/IgM (without diff. of IgG and IgM)"
- "Status of hantavirus infection (without differentiation of serotype)"
- "Serotype differentiation (only accepted together with infection status)"

All results should be reported according to the requests of the entry mask in EQAS Online.

The results should be reported as "positive", "negative", or "borderline"/"indeterminate".

Titers, concentrations (Units/volume) as well as **raw data of your analyses** as S/CO, Index etc. should be reported separately. We will start to show these raw data in the final reports in due time.

When applying **immunoblots** please report the detected antibodies against the corresponding hantavirus specific antigens.

In case of positive detection of a hantavirus antigen please report the **band intensity and grade** if possible the intensity as e.g. **(+++), (++)**, **(+)** or **(+/-)** and **(0)** for **negative**.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline:

18.09.2020

Virus Immunology Hepatitis A Virus (343)

anti-HAV-IgG/IgM

subject to RiliBAEK B 2

September 2020

Instructions for test performance

Samples **343165, 343166:** anti-HAV
343167, 343168: anti-HAV-IgM
sera (0.5 ml each)

Precautions

The sera are negative for HIV, HBV and HCV (by serology). The samples are not heat inactivated and must be considered and treated as potentially infectious. Samples positive for virus specific IgM are potentially infectious for the corresponding virus. All sera must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples should be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

Please note the "**Instructions for Virus Immunology**". The samples are non-lyophilized sera (0.5 ml each) and should be **centrifuged preferentially at 10,000 RCF** (Relative Centrifugal Force) for **10 min between +4°C and +8°C**. At least standard centrifugation conditions for serum preparation (for removing the clot) should be applied.

Test performance and result entry to EQAS Online (= "RV-Online") system

Both samples of a sample pair (even a negative sample) have to be analyzed using the **same test**: the samples **343165** and **343166** for anti-HAV, the samples **343167** and **343168** for anti-HAV-IgM. Qualitative analyses should be performed for all samples under standard conditions. No titration is needed.

Parameter:

- "Anti-HAV IgG"
- "Anti-HAV IgM"

All results should be reported according to the requests of the entry mask in EQAS Online.

Titers, concentrations (Units/volume) as well as **raw data of your analyses** as S/CO, Index etc. should be reported separately. We will start to show these raw data in the final reports in due time.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: **18.09.2020**

Virus Immunology Hepatitis B Virus (344) (Program 1)

HBsAg

anti-HBs

anti-HBc

subject to RiliBAEK B 3

subject to RiliBAEK B 2

subject to RiliBAEK B 2

September 2020

Instructions for test performance

Samples **344493, 344494, 344495, 344496:** HBsAg
344497, 344498, 344499, 344500: anti-HBs
344501, 344502, 344503, 344504: anti-HBc
sera (HBsAg: 1.0 ml each)
(anti-HBs: 0.75 ml each)
(anti-HBc: 0.75 ml each)

Precautions

The samples **344493, 344494, 344495** and **344496** are potentially HBsAg positive and can be infectious for HBV; the samples **344497, 344498, 344499** and **344500** are HBsAg negative; the samples **344501, 344502, 344503** and **344504** may be **positive for HBsAg and anti-HBc-IgM and can be infectious for HBV depending on the status of infection**.

All sera are negative for HIV and HCV (by serology). The sera are not heat inactivated. All sera must be considered and treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples and test performance

Please note the "**Instructions for Virus Immunology**". **All samples of a sample set** (even a negative sample) should be analyzed applying the **same tests**.

Parameter "HBsAg qualitative"

and

Parameter "HBsAg qualitative and results in IU/ml"

Please note the "**Instructions for Virus Immunology**".

The samples **344493, 344494, 344495** and **344496** (1.0 ml each) are non-lyophilized sera and should be **centrifuged preferentially at 10,000 RCF** (Relative Centrifugal Force) for **10 min between +4°C and +8°C**. At least standard centrifugation conditions for serum preparation (for removing the clot) should be applied.

Qualitative analyses should be performed for all samples with tests routinely used in your laboratory under standard conditions of the test kit.

The parameter for tests, which detect HBsAg exclusively qualitative, is available on the entry mask as "HBsAg qualitative".

Qualitative results have to be reported as "reactive / positive", "non-reactive / negative", or "borderline".

The parameter for tests, which state the result in IU/ml, is available on the entry mask as "HBsAg qualitative and specification in IU/ml".

Quantitative results have to be reported in International Units/ml (IU/ml) and have to be interpreted qualitatively as "reactive / positive", "non-reactive / negative", or "borderline".

Please note that we ask you to report also the **raw data of your analyses** (e.g. s/co, index etc.). We will start to show these raw data in the final reports in due time.

Parameter "Confirmation test HBsAg"

HBsAg reactive results should be confirmed in a confirmation test. In this case, please fill in your final result into the section "Final results" which should be reported as "positive", "negative" or "borderline".
Samples which are HBsAg negative in the primary screening test should not be analyzed by confirmation tests.

Parameter "Anti-HBs"

Please note the "**Instructions for Virus Immunology**". The samples **344497, 344498, 344499** and **344500** are non-lyophilized sera (0.75 ml each) and should be **centrifuged preferentially at 10,000 RCF** (Relative Centrifugal Force) for **10 min between +4°C and +8°C**. At least standard centrifugation conditions for serum preparation (for removing the clot) should be applied.

All sera should be analyzed for anti-HBs applying all tests routinely used in your laboratory (even for a negative sample).

The results have to be reported as "positive" or "non-reactive"/"negative". **Concentrations for anti-HBs should be reported in International Units per liter (IU/l) and have to be linked with a qualitative result ("reactive/positive" or "non-reactive/negative").** Please note: concentrations with ">" are not accepted for positive samples.

For the interpretation of your result for anti-HBs stated in IU/l please consider the "Recommendations of the Standing Committee on Vaccination (STIKO) at the Robert Koch Institute – 2017/2018", especially the indication for hepatitis B immune prophylaxis after exposure with HBV contaminated materials, e.g. after needle stick injury (https://www.rki.de/EN/Content/infections/Vaccination/recommendation/s/34_2017_engl.pdf?blob=publicationFile). Updated recommendation in German language (2020): https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2020/Ausgaben/34_20.pdf?blob=publicationFile

Parameter "Anti-HBc"

Please note the "**Instructions for Virus Immunology**". The samples **344501, 344502, 344503** and **344504** are non-lyophilized sera (0.75 ml each) and should be **centrifuged preferentially at 10,000 RCF** (Relative Centrifugal Force) for **10 min between +4°C and +8°C**. At least standard centrifugation conditions for serum preparation (for removing the clot) should be applied.

Qualitative analyses should be performed for all samples with all tests routinely used in your laboratory under standard conditions of the test kit. No titration is needed. Qualitative results have to be reported as "reactive / positive", "non-reactive / negative", or "borderline".

Please note that we ask you to report also the **raw data of your analyses** (e.g. s/co, index etc.). We will start to show these raw data in the final reports in due time.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: **18.09.2020**

Virus Immunology Hepatitis B Virus (345) (Program 2)

anti-HBc-IgM

subject to RiliBAEK B 2

HBeAg

subject to RiliBAEK B 3

anti-HBe

subject to RiliBAEK B 2

September 2020

Instructions for test performance

Samples 345247, 345248: anti-HBc-IgM
345249, 345250: HBeAg
345251, 345252: anti-HBe
sera (0.5 ml each)

Precautions

The sera are potentially positive for HBsAg, i.e. potentially infectious for HBV, but negative for HIV and HCV (by serology), respectively. The samples are not heat inactivated. All sera must be considered and treated as potentially infectious material and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples should be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

Please note the "**Instructions for Virus Immunology**". The samples are non-lyophilized sera (0.5 ml each) and should be **centrifuged preferentially at 10,000 RCF** (Relative Centrifugal Force) for **10 min between +4°C and +8°C**. At least standard centrifugation conditions for serum preparation (for removing the clot) should be applied.

Test performance and result entry to EQAS Online (= "RV-Online") system

Both samples of a sample pair (even a negative sample) should be analyzed using the **same test**: the samples **345247** and **345248** for anti-HBc-IgM (0.5 ml) (**please note that a test for the detection anti-HBc is not sufficient**), the samples **345249** and **345250** for HBeAg (0.5 ml), the samples **345251** and **345252** for anti-HBe (0.5 ml). Qualitative analyzes should be performed for all samples under standard conditions. No titration is needed.

Parameter:

- "Anti-HBc IgM"
- "HBeAg"
- "Anti-HBe"

All results should be reported according to the requests of the entry mask in EQAS Online.

Titers, concentrations (Units/volume) as well as **raw data of your analyses** as S/CO, Index etc. should be reported separately. We will start to show these raw data in the final reports in due time.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: **18.09.2020**

Virus Immunology Hepatitis C Virus (346)

anti-HCV
HCV antigen

subject to RiliBAEK B 2
subject to RiliBAEK B 3

September 2020

Virus Immunology HIV-1/HIV-2 (335)

anti-HIV-1/2

subject to RiliBAEK B 2

September 2020

Instructions for test performance

Samples **346165, 346166, 346167, 346168**
sera (0.5 ml each)

Precautions

The serum and plasma samples are negative for HIV and HBV (by serology). The samples are not heat inactivated. All sera must be considered and treated as potentially infectious for HCV and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples should be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

Please note the "**Instructions for Virus Immunology**". The samples are non-lyophilized serum and plasma samples (0.5 ml each) should be **centrifuged preferentially at 10,000 RCF** (Relative Centrifugal Force) for **10 min between +4°C and +8°C**. At least standard centrifugation conditions for serum preparation (for removing the clot) should be applied.

Test performance and result entry to EQAS Online (= "RV-Online") system

The samples should be analyzed qualitatively in tests for the detection of antibodies against hepatitis C virus (anti-HCV) or tests for the combined detection of anti-HCV and HCV antigen under standard conditions. No titration is needed.

All samples (even a negative sample) should be analyzed using the **same test kit**.

Parameter:

- "Screening test anti-HCV and combined detection anti-HCV and HCV antigen"
- "HCV antigen"
- "Complementary test (blot) anti-HCV"

All results should be reported according to the requests of the entry mask in EQAS Online.

Titers, concentrations (Units/volume) as well as **raw data of your analyses** as S/CO, Index etc. should be reported separately. We will start to show these raw data in the final reports in due time.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: **18.09.2020**

Instructions for test performance

Samples **335165, 335166 335167, 335168**
sera (0.75 ml each)

Precautions

The sera are positive for anti-HIV-1 or anti-HIV-2 and negative for HBV and HCV (by serology). The samples were not heat inactivated and must be considered and treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples should be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

Please note the "**Instructions for Virus Immunology**". The samples are non-lyophilized sera (0.75 ml each) and should be **centrifuged preferentially at 10,000 RCF** (Relative Centrifugal Force) for **10 min between +4°C and +8°C**. At least standard centrifugation conditions for serum preparation (for removing the clot) should be applied.

In case of **rapid tests for anti-HIV** the centrifugation step can be dispensed.

Test performance and result entry to EQAS Online (= "RV-Online") system

The sera should be analyzed for anti-HIV-1 and anti-HIV-2 with your routine tests under standard conditions.

For confirmation testing all samples (also negative samples) should be analyzed by the **same tests**.

Parameter:

- "Screening test anti-HIV-1 / anti-HIV-2 (3rd and 4th generation)"
- "Confirmation test (blot and other confirmatory test) anti-HIV-1 / anti-HIV2"
- "Confirmation test (blot and other confirmatory test) anti-HIV-1"
- "Confirmation test (blot and other confirmatory test) anti-HIV-2"

All results should be reported according to the requests of the entry mask in EQAS Online.

Please note that we ask you to report also the **raw data of your analyses** (e.g. s/co, index etc.). We will start to show these raw data in the final reports in due time.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: **18.09.2020**

Virus Immunology HIV-1 p24 antigen (337)

HIV-1 p24 antigen *subject to RiliBAEK B 3*

September 2020

Virus Immunology SARS-CoV-2 (416)

anti-SARS-CoV-2 *conform to RiliBAEK B 3*

September 2020

Instructions for test performance

Samples **337083, 337084**
sera (0.75 ml each)

Precautions

The samples contain sera negative for HIV, HBV and HCV (by serology) which were spiked with purified HIV-1 (virus heat inactivated). Negative sera were not heat inactivated. All sera must be considered and treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples should be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

Please note the "**Instructions for Virus Immunology**". The samples are non-lyophilized sera (0.75 ml each) and should be **centrifuged preferentially at 10,000 RCF** (Relative Centrifugal Force) for **10 min between +4°C and +8°C**. At least standard centrifugation conditions for serum preparation (for removing the clot) should be applied.

In case of **rapid tests for anti-HIV** the centrifugation step can be dispensed.

Test performance and result entry to EQAS Online (= "RV-Online") system

The sera should be analyzed for p24 antigen applying all tests routinely used. Qualitative results should be stated as "reactive"/"positive", "non-reactive"/"negative" or "borderline". Test results of quantitative analyses should be stated in picogram (pg/ml).

Parameter:

- "HIV-1 p24 Ag"
- "HIV-1 p24 Ag confirmation test"

All results should be reported according to the requests of the entry mask in EQAS Online.

Titers, concentrations (Units/volume) as well as **raw data of your analyses** as S/CO, Index etc. should be reported separately. We will start to show these raw data in the final reports in due time.

Attention! In case you use screening tests, please be aware that only 4th generation tests detecting p24 antigen in addition to anti-HIV-1 and anti-HIV-2 are suitable for this EQA scheme.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: **18.09.2020**

Instructions for test performance

Samples **native patient serum**
(0.5 ml each)

Each participant receives a defined panel of samples with sera from whole blood or plasma (not re-calcified). Each panel member contains patient serum or patient plasma from **one individual donor only**.

Please note:

Due to the high number of registrations, INSTAND e.V. has split the EQA group 416 into three subgroups. Please check on your delivery note which subgroup number has been assigned to you.

Subgroup 4161	Sample matrix
416013	serum
416014	serum
416015	serum
416016	serum

Subgroup 4162	Sample matrix
416017	serum
416018	serum
416019	serum
416020	serum

Precautions

The serum and plasma samples are negative for HIV, HBV and HCV (by serology) and **negative for SARS-CoV-2 RNA**. The samples are not heat inactivated and must be considered and treated as potentially infectious. All samples must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples should be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

Please note the "**Instructions for Virus Immunology**". The samples are non-lyophilized serum or plasma samples (0.5 ml each) and should be **centrifuged preferentially at 10,000 RCF** (Relative Centrifugal Force) for **10 min between +4°C and +8°C**. At least standard centrifugation conditions for serum preparation (for removing the clot) should be applied.

Test performance

The samples should be analyzed for antibodies against SARS-CoV-2 applying tests routinely used in your laboratory (even for a negative sample). Please analyze each of the four samples of your subgroup with one or more tests for one or more of the following parameters.

Parameter:

- "Anti-SARS-CoV-2 total (without differentiation of IgG, IgA and IgM)"
- "Anti-SARS-CoV-2 IgG"
- "Anti-SARS-CoV-2 IgG - avidity"
- "Anti-SARS-CoV-2 IgA"
- "Anti-SARS-CoV-2 IgM"
- "Clinical interpretation"

All results should be reported according to the requests of the entry mask in EQAS Online.

Concentrations (units/volume), titers as well as **raw data of your analyses** as S/CO, index etc. should be reported separately.

Clinical interpretation of the tested samples

For the clinical evaluation, we refer to the following illustration on page 7 (Sethuraman N, Jeremiah SS, Ryo A. Interpreting Diagnostic Tests for SARS-CoV-2. JAMA. Published online May 06, 2020.

<http://jamanetwork.com/article.aspx?doi=10.1001/jama.2020.8259>).

Consider the performance spectrum of the test or test combination you are using and indicate whether the corresponding sample is typical for:

- "status after acquired infection"
- "recently acquired infection"
- "past infection"
- "by serology no sign for infection"
- "infection status unclear"

Result entry to EQAS Online system

Follow the assigned **subgroup number** in the INSTAND EQAS Online system

<https://rv-online.instandev.de/index.shtml?lang=en>

Deadline: **02.10.2020**

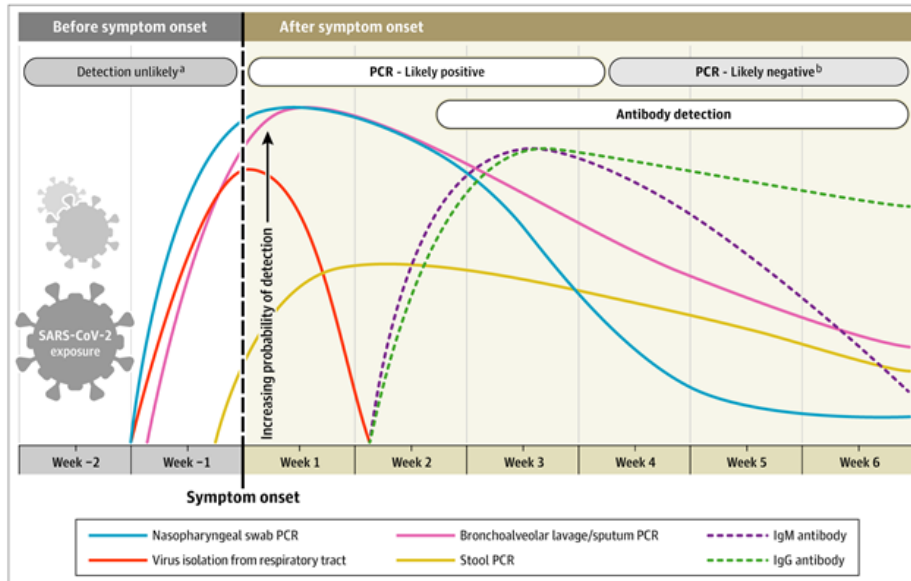


Figure Legend:

Estimated Variation Over Time in Diagnostic Tests for Detection of SARS-CoV-2 Infection Relative to Symptom Onset. Estimated time intervals and rates of viral detection are based on data from several published reports. Because of variability in values among studies, estimated time intervals should be considered approximations and the probability of detection of SARS-CoV-2 infection is presented qualitatively. SARS-CoV-2 indicates severe acute respiratory syndrome coronavirus 2; PCR, polymerase chain reaction.

^aDetection only occurs if patients are followed up proactively from the time of exposure.

^bMore likely to register a negative than a positive result by PCR of a nasopharyngeal swab.

Virus Immunology Rabies Virus (336)
anti-RABV *conform to RiliBÄK B 2*
September 2020

Instructions for test performance

Samples 336013, 336014
sera (0.5 ml each)

Precautions

The sera are negative for HIV, HBV and HCV (by serology). The antibody positive sera derive from rabies vaccinee. The samples are not heat-inactivated and must be considered and treated as potentially infectious. All sera must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples should be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

Please note the "**Instructions for Virus Immunology**". The samples are non-lyophilized sera (0.5 ml each) and should be **centrifuged at least at 10,000 RCF** (Relative Centrifugal Force) for **10 min between +4°C and +8°C**.

Test performance and result entry to EQAS Online (= "RV-Online") system

The samples should be analyzed for antibodies against rabies virus applying all tests routinely used in your laboratory (even for a negative sample).

Parameter:

- "Anti-rabies virus"

All results should be reported according to the requests of the entry mask in EQAS Online.

Titers, concentrations (Units/volume) as well as **raw data of your analyses** as S/CO, Index etc. should be reported separately. We will start to show these raw data in the final reports in due time.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: **18.09.2020**

Virus Immunology Zika virus (338)
anti-ZIKV-IgG/IgM *conform to RiliBAEK B 2*
September 2020

Instructions for test performance

Samples 338022, 338023, 338024
sera (0.3 ml each)

Precautions

The sera are negative for HIV, HBV and HCV (by serology) and also negative for ZIKV RNA. The samples are not heat inactivated and must be considered and treated as potentially infectious. All sera must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples should be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

Please note the "**Instructions for Virus Immunology**". The samples are non-lyophilized sera (0.3 ml each) and should be **centrifuged preferentially at 10,000 RCF** (Relative Centrifugal Force) for **10 min between +4°C and +8°C**. At least standard centrifugation conditions for serum preparation (for removing the clot) should be applied.

Test performance and result entry to EQAS Online (= "RV-Online") system

The samples should be analyzed for IgG and IgM antibodies against Zika virus (anti-ZIKV-IgG/anti-ZIKV-IgM) or for total antibodies against Zika virus (anti-ZIKV-total) applying all tests routinely used in your laboratory (even for a negative sample).

Parameter:

- "Anti-ZIKV IgG"
- "Anti-ZIKV IgG – avidity"
- "Anti-ZIKV IgM"

All results should be reported according to the requests of the entry mask in EQAS Online.

Titers, concentrations (Units/volume) as well as **raw data of your analyses** as S/CO, Index etc. should be reported separately. We will start to show these raw data in the final reports in due time.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: **18.09.2020**

VIRUS GENOME DETECTION

Instructions for Virus Genome Detection

1. Storage of samples

The samples should be stored in a refrigerator (+2°C to +8°C) directly after receipt.

2. Pre-treatment of samples for virus genome detection

The EQAS samples for virus genome detection by PCR/NAT are lyophilized materials of the corresponding viruses (matrix: plasma, serum, tissue culture medium, suspension of feces, suspension of urine; please see the corresponding EQA program).

As the lyophilizates may be fluffy it is advised to concentrate the fluffy material by short centrifugation (e.g. run up to speed in an Eppendorf table desk centrifuge followed by immediate stop).

The EQAS samples for virus genome detection by PCR/NAT should be reconstituted by careful addition of the corresponding volume of aqua bidest. (sterile, pyrogen-free, PCR-grade) by vigorous mixing (Vortex) for 20 min at room temperature. Mixing should be repeated until complete reconstitution of the sample material.

After reconstitution the sample should **not be centrifuged**. The subsequent nucleic acid extraction of the samples should be performed immediately and according to the manufacturer's instructions.

2.1 Special instruction for the application of FTA cards

Please note for the EQA program for virus genome detection of measles virus, mumps virus and rubella virus, respectively.

The cell lysates are immobilized on sample disks (FTA card). Potentially infectious viruses are chemically inactivated on the sample disk. Each sample disk (FTA card) should be reconstituted in 1.1 ml Aqua bidest. (sterile, pyrogen-free, PCR-grade) by vigorous mixing (Vortex) for 20 min at room temperature. After reconstitution the samples should **not be centrifuged!** The subsequent nucleic acid extraction of the samples should be performed immediately and according to the manufacturer's instructions.

2.2 Special instruction for blood banks

We would like to inform you that virus genome analyses by PCR/NAT should be performed **without further dilution** of the EQAS samples after reconstitution in aqua bidest. Especially colleagues performing virus safety testing of blood and blood products (e.g. blood banks testing with PCR/NAT for HIV, HBV, HCV, CMV, parvovirus B19 etc) are asked **NOT TO DILUTE** the EQAS samples **in pools**. Only quantitative test results obtained from undiluted samples can be evaluated in the context with the results of all participants and considered for your certificate.

Attention!

2.3 Information on INSTAND EQA scheme Virus genome detection – Hepatitis C Virus Geno- / Subtyping (375)

Subtyping of Hepatitis C Virus (HCV) genotype 1 viruses required

The updated EASL Recommendations on Treatment of Hepatitis C 2018, European Association for the Study of the Liver, Journal of Hepatology, 2018 (<https://easl.eu/wp-content/uploads/2018/10/HepC-English-report.pdf>) states: "The HCV genotype and genotype 1 subtype (1a or 1b) must be assessed prior to treatment initiation to determine the choice of therapy and its duration, among other parameters."

This is in agreement with the "S3-Leitlinie der AWMF - Prophylaxe, Diagnostik und Therapie Hepatitis-C-Virus(HCV)-Infektion", (AWMF-Registernummer 021/012)

https://www.awmf.org/uploads/tx_szleitlinien/021-012l_S3_Hepatitis-C-Virus_HCV-Infektion_2018-07.pdf

We want to inform you that, since September 2015, it is necessary to state the HCV subtype 1a or 1b for samples containing HCV genotype 1. The differentiation between the HCV subtypes 1a and 1b is a prerequisite for obtaining a certificate of successful participation.

This means that for samples with HCV genotype 1, the exclusive statement "genotype 1" is not sufficient for successful participation in this EQA scheme.

2.4 Application of the APTIMA HPV assay from Gen-Probe for the detection of human papilloma viruses (HPVs)

PLEASE NOTE! As stated in the instructions for test performance for the EQA program "PCR/NAT HPV" (373) the lyophilized test samples should be reconstituted in **1.1 ml Specimen Transport Media (STM, Gen-Probe)** taken from Specimen Transfer Tube (2.9 ml STM). The samples should be reconstituted for 20 min at room temperature. Complete mixture of the lyophilisate should be ensured by gently inverting the tube 2 to 3 times. Please do not mix vigorously (vortex) to avoid foam formation.

The reconstituted samples (1.1 ml) should be transferred back into the respective Specimen Transfer Tube to obtain a final volume of 2.9 ml. Shake the tube gently for mixing (do not mix with Vortex).

All following steps of the test procedure should be performed according to the manufacturer's instructions.

2.5 Application of the HC2 HPV DNA tests from Qiagen for the detection of human papilloma viruses (HPVs)

PLEASE NOTE! Differing from the manufacturer's instructions for analysis of biopsy materials and smear tests (HC2 HPV DNA test) you should reconstitute the lyophilized EQAS samples in **1.1 ml Specimen Transport Medium (Qiagen)**.

The samples have to be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently **0.55 ml Denaturing Reagent (Qiagen)** will be added and all following steps of the test procedure should be performed according to the manufacturer's instructions for the HC2 HPV DNA test.

2.6 Application of the Xpert HPV Assay of Cepheid for the detection of human papillomavirus

PLEASE NOTE! As stated in the instructions for test performance for the EQA program "PCR/NAT Human Papillomavirus" (373) the samples should be reconstituted in 1.1 ml aqua bidest (sterile, pyrogen-free, PCR-grade).

Follow now the manufacturer's instructions: Please transfer 1.0 ml of the resuspended specimen into the reagent bottle (sample vial) containing 20 ml of PreservCyt solution (Hologic Corporation). The closely capped reagent bottle should be mixed by gently inverting the reagent bottle eight to ten times, or by vortexing briefly with a vortex mixer at half speed continuously for five seconds in accordance to the manufacturer's instructions. **After mixing 1.0 ml of the sample should be transferred using the transfer pipette into the Xpert HPV Assay cartridge** (ensure that the pipette is filled without air bubbles). Thereafter, testing should be performed in accordance to the manufacturer's instructions.

2.7 Application of the Xpert Norovirus Assay of Cepheid for the detection of noroviruses

PLEASE NOTE! As stated in the instructions for test performance for the EQA program "PCR/NAT Norovirus" (381) the suspensions of feces should be reconstituted in 1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade).

Please transfer 1.0 ml of the resuspended specimen into the sample reagent bottle. The closely capped sample reagent bottle should be mixed at high speed for 10 seconds (Vortex) in accordance to the manufacturer's instructions. **After mixing 2.0 ml of the sample should be transferred to the Xpert Norovirus Assay cartridge.** Thereafter, testing should be performed in accordance to the manufacturer's instructions.

2.8 Application of the Xpert Flu/RSV XC Assay and Xpert Xpress Flu/RSV Assay of Cepheid for the detection of influenza viruses and RSV

PLEASE NOTE! As stated in the instructions for test performance for the EQA programs "Influenza A and B viruses" (370) and "Respiratory syncytial virus" (359) the samples should be reconstituted in 1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade). Please transfer 600 µl of the resuspended specimen into the "3ml vial" containing Xpert Viral Transport Medium. Thereafter, testing should be performed in accordance to the manufacturer's instructions.

3. Test performance

See following instructions for test performance for the corresponding EQA program.

3.1 Nucleic acid extraction for PCR/NAT

In dependence of the EQA program the samples comprise different materials from different sources, e.g. plasmas, sera, cell lysates, biopsy materials, suspensions of feces or urine. Please follow the instructions of each corresponding EQA program. Please note:

- In case of application a commercial test kit including reagents for extraction, please follow the instructions of the manufacturer.
- In case you use a separate commercial extraction kit please consider the nature of the viral nucleic acid (RNA or DNA) as well as the specimen from which the nucleic acid should be extracted (e.g. plasma, cell lysate or biopsy material).
- Please indicate the name and the lot-no. of the extraction kit in the corresponding entry mask in EQAS Online.

4. Reporting of results

4.1 Reporting of quantitative results

Quantitative results (IU/ml or copies/ml) should be stated as numerical values under "Result (quant)" of the entry mask.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows: Consider the limit of detection of your test system (e.g. 50 IU/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please note the following:

Evaluation of results for quantitative genome detection of CMV

Notice for German and foreign participants of EQA scheme 365:

For evaluation, "IU/ml" have primarily been considered as measurement units of the quantitative results for the analyte CMV. This is in accordance to the "Guidelines of the German Medical Association (Bundesärztekammer / RiliBÄK)", Specified RiliBÄK Section B 3, Table B. 3-2a,

When applying CE-marked tests, which not (yet) allow reporting of results in IU/mL, it should be continued to report the results as stated by the manufacturer.

Evaluation of results for quantitative genome detection of HBV and HCV

Notice for German participants of EQA schemes 361 and 362:

For evaluation, "IU/ml" have been considered as measurement units of the quantitative results for the analytes HBV and HCV. This is in accordance to the "Guidelines of the German Medical Association (Bundesärztekammer / RiliBÄK)", Specified RiliBÄK Section B 3, Table B. 3-2a. Statements in "copies/ml" will not be accepted anymore.

Notice for foreign participants of EQA schemes 361 and 362:

Please note that quantitative results in "copies/ml" for the genome detection of HBV and HCV, respectively, have not been evaluated due to the low number of analyses.

Evaluation of results for quantitative genome detection of HIV-1 (RNA)

Notice for German participants of EQA scheme 360:

For evaluation, "copies/ml" have been considered as measurement unit of the quantitative results for the analyte HIV-1 (RNA). This is in accordance to the "Guidelines of the German Medical Association (Bundesärztekammer / RiliBÄK)", Specified RiliBÄK Section B 3, Table B. 3-2a.

Statements in "IU/ml" will not be accepted anymore.

Notice for foreign participants of EQA scheme 360:

Please note that quantitative results in "IU/ml" for the genome detection of HIV-1 (RNA) have not been evaluated due to the low number of analyses.

4.2 Reporting of qualitative results

Please report in the corresponding parameter for virus genome detection only results, obtained exclusively by qualitative PCR/NAT. Please do not report a qualitative interpretation from a quantitative PCR/NAT result.

4.3 Reporting of Ct/Cp-values

Please report the Ct-value (cycle threshold) or Cp-value (crossing point) under "Device value" and "Unit (device value)" depending on your thermo-cycler in case you performed a Real-Time-PCR.

4.4 Simultaneous reporting of different results

The simultaneous reporting of different results for one and the same sample can not be accepted and will be evaluated as a missing value, e.g. the **simultaneous reporting** of a "positive" and "indeterminate" result will not be accepted.

4.5 Reporting of results obtained with different tests

In order to get a comprehensive evaluation of all tests performed in the different laboratories it is necessary to collect as many results as possible. In case you receive deviating results for a given sample by applying tests from different manufacturers, please indicate which of the results should be considered for your certificate.

4.6 Analyzing negative samples

All samples of a sample set (also negative samples) have to be analyzed with all methods routinely used in your laboratory. Please keep in mind that only this strategy will allow the detection of **problems of sensitivity and specificity** for the different tests and methods. In case you get discrepant results by this approach, you can indicate this observation without any disadvantages for your certificate.

PCR/NAT - BK Virus (364)
BK Virus DNA conform to RiliBÄK B 3
September 2020

Detection of BK virus by PCR and other nucleic acid techniques (NAT)

Instructions for test performance

Samples 364053, 364054, 364055, 364056
lyophilized suspensions of urine
(1.1 ml each)

Precautions

The suspensions of urine are potentially positive for BK virus and not tested for HIV, HBV and HCV genomes, respectively. The samples are not inactivated. All samples must be considered and treated as potentially infectious materials and must be used only for experimental/diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "Instructions for Virus Genome Detection"
The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying the tests for the detection of BK virus genome routinely used in your laboratory (even for a negative sample).

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The DNA of BK virus should be analyzed quantitatively and/or qualitatively. Please apply your routine tests and report all necessary information according to the entry mask in EQAS Online.

If you use different tests for quantitative and qualitative genome detection please report the results in the corresponding parameters of the entry mask. Please do not report a qualitative interpretation from a quantitative PCR/NAT result.

Parameter:

- "BK virus (DNA) - quantitative"
- "BK virus (DNA) - qualitative"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct-/Cp-values are requested.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows: Consider the limit of detection of your test system (e.g. 50 copies/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: 18.09.2020

PCR/NAT - Chikungunya Virus (392)
CHIKV RNA conform to RiliBÄK B 3
September 2020

Detection of chikungunya virus (CHIKV) by PCR and other nucleic acid techniques (NAT)

Instructions for test performance

Samples 392045, 392046, 392047, 392048
lyophilized cell lysates (1.1 ml each)

The EQA scheme may contain current circulating outbreak strains.

Precautions

The specimens (negative for HIV, HBV and HCV, respectively) contain inactivated chikungunya viruses. All samples must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "Instructions for Virus Genome Detection"
The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying your routine tests for the detection of chikungunya virus genome (even for a negative sample).

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The RNA of chikungunya virus should be analyzed quantitatively and/or qualitatively. Please apply your routine tests and report all necessary information according to the entry mask in EQAS Online.

If you use different tests for quantitative and qualitative genome detection please report the results in the corresponding parameters of the entry mask.

Please do not report a qualitative interpretation from a quantitative PCR/NAT result.

Parameter:

- "CHIKV (RNA) - quantitative"
- "CHIKV (RNA) - qualitative"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct-/Cp-values are requested.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows: Consider the limit of detection of your test system (e.g. 50 copies/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: 18.09.2020

PCR/NAT - Cytomegalovirus (365)
CMV DNA *subject to RiliBAEK B 3*
September 2020

Detection of cytomegalovirus (CMV) by PCR and other nucleic acid techniques (NAT)

Instructions for test performance

Samples **365165, 365166, 365167, 365168**
lyophilized plasmas (1.1 ml each)

Precautions

The samples are potentially positive for CMV and negative for HIV, HBV and HCV (by serology). The samples are not inactivated. All samples must be treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "Instructions for Virus Genome Detection"
 The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying the tests for the detection of CMV genome routinely used in your laboratory (even for a negative sample).

Please note! Each sample should be tested as individual sample and **not be diluted in pools**.

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The CMV genome should be detected quantitatively and/or qualitatively. Please apply your routine tests and report all necessary information according to the entry mask.

Parameter "CMV (DNA) - quantitative"

All results should be reported according to the requests of the entry mask in EQAS Online.

As already announced, the statements for reporting quantitative results of virus genome detection should be given in accordance to the Specified RiliBÄK Section B 3; Table B 3-2a, column 4.

Therefore, the quantitative results for CMV should be reported primarily as International Units (IU)/ml.

Please note:

When applying CE-marked tests, which not (yet) allow reporting of results in IU/ml, it should be continued to report the results as stated by the manufacturer.

If your test system reports "below level of detection" as quantitative result, please proceed as follows:

Consider the limit of detection of your test system (e.g. 50 IU/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Parameter "CMV (DNA) - qualitative"

All results should be reported according to the requests of the entry mask in EQAS Online.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: **18.09.2020**

PCR/NAT - (349)
CMV resistance determination
CMV resistance *conform to RiliBAEK B 3*
September 2020

Polymerase Chain Reaction (PCR), other nucleic acid amplification techniques (NAT) and sequencing for CMV resistance determination

Instructions for test performance

Samples:

DNA eluate in water liquid 100 µl

Sample No.	resistance determination in gene region
349021	UL97 and UL54

Virus in plasma lyophilized 1100 µl

Sample No.	resistance determination in gene region
349022	UL97 and UL54
349023	UL97 and UL54
349024	UL97 and UL54

Negative samples are not supplied.

Precautions

The samples are positive for CMV and negative for HIV, HBV and HCV (by serology), respectively. The samples are not inactivated. All samples must be treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

Virus in plasma lyophilized 1100 µl

The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying the tests for the amplification of CMV genome and genotypic CMV resistance determination routinely used in your laboratory.

DNA eluate in water liquid 100 µl

DNA eluate can be applied directly for amplification and genotypic resistance determination of CMV (without extraction).

You receive **2 tubes** of each sample.

Test performance and submission of results

Starting with the EQA term November/December 2018, reporting of resistance results is possible for two gene regions:

- **UL97-gene region**
- **UL54-gene region**

Results of resistance testing will independently be certified for each of the gene regions.

Please apply your routine tests for the extraction, amplification and genotypic resistance determination of gene region UL97 and/or gene region UL54 and report all necessary information according to the protocol.

Statements on individual parameters

Parameter 10, 20 and 30 for resistance testing in UL97
Parameter 40, 50 and 60 for resistance testing in UL54

10./40. Sequence determination for the interpretation of the genotypic resistance

Starting with the EQA term November/December 2019, reporting of your results for the sequence determination are mandatory, but are not a prerequisite for receiving a "certificate" in this EQA scheme.

Please send your sequence data as text or FASTA files stating as file name "sample number_INSTAND participant number/TN number" (e.g. 349022_TN1234) together with the Excel file.

20./50. Determination of resistance-associated mutations

The results should be reported as amino acid exchange and the position of the resistance-associated mutations (e.g. H520Q). Only statements on **confirmed** resistance-associated mutations are requested. **Statements of additional mutations (e.g. polymorphisms) can be evaluated as "false"**.

The results for the determination of resistance-associated mutations will be evaluated.

30./60. Interpretation of genotypic resistance

Please report the interpretation of the genotypic resistance against virostatics as follows:

- susceptible (= no restricted drug efficacy)
- resistant (= restricted drug efficacy)

The results for the interpretation of the genotypic resistance will be evaluated.

Electronic protocol – submission

Please use **the electronic protocol (excel file)** for reporting your results for this EQA scheme. The electronic protocol is available for **download**:
<http://www.instand-ev.de/virus-resistance>

Please note:

State your **INSTAND participant number** in the electronic protocol.

The electronic protocol should be submitted directly to:
Heinz.Zeichhardt@iqvd.de

Deadline: **23.10.2020**

Scientific cooperation partners for this EQA scheme

Nationales Konsiliarlaboratorium für Cytomegalievirus (Schwerpunkt) CMV-Infektionen bei immunsupprimierten Personen
Universitätsklinikum Ulm
Prof. Dr. T. Stamminger
Prof. Dr. D. Michel

Nationales Konsiliarlaboratorium für Cytomegalievirus (Schwerpunkt) kongenitale/postnatale CMV-Infektionen
Universitätsklinikum Tübingen
Prof. Dr. T. Iftner
Prof. Dr. K. Hamprecht

PCR/NAT - Dengue Viruses (369)

DENV RNA *conform to RiliBÄK B 3*
September 2020

Detection of dengue viruses (DENV) by PCR and other nucleic acid techniques (NAT) with the option of typing

Instructions for test performance

Samples **369053, 369054, 369055, 369056**
lyophilized cell lysates (1.1 ml each)

Precautions

The specimens (negative for HIV, HBV and HCV, respectively) contain inactivated dengue viruses. All samples must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "**Instructions for Virus Genome Detection**"

The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying your routine tests for the detection of dengue virus genome (even for a negative sample). In case of positive samples please determine the dengue virus type.

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The RNA of dengue virus should be analyzed quantitatively and/or qualitatively. In addition, please determine the dengue virus type. Please apply your routine tests and report all necessary information according to the entry mask in EQAS Online. If you use different tests for quantitative and qualitative genome detection please report the results in the corresponding parameters of the entry mask. Please do not report a qualitative interpretation from a quantitative PCR/NAT result.

Parameter:

- "Dengue virus (RNA) - quantitative"
- "Dengue virus (RNA) - qualitative"
- "Dengue virus (RNA) - type identification"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct-/Cp-values are requested.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows: Consider the limit of detection of your test system (e.g. 50 copies/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: **18.09.2020**

PCR/NAT - Hepatitis A Virus (377)HAV RNA *subject to RiliBAEK B 3***September 2020**

Detection of hepatitis A virus (HAV) by PCR and other nucleic acid techniques (NAT)

Instructions for test performance

Samples 377165, 377166, 377167, 377168
lyophilized plasmas (1.1 ml each)

Precautions

The plasmas are potentially positive for HAV and negative for HIV, HBV and HCV (by serology), respectively. The samples are not inactivated. All samples must be considered and treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "**Instructions for Virus Genome Detection**"
The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying the tests for the detection of HAV genome routinely used in your laboratory (even for a negative sample).

Please note! Each sample should be tested as individual sample and **not be diluted in pools**.

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The RNA of HAV should be analyzed quantitatively and/or qualitatively. Please apply your routine tests and report all necessary information according to the entry mask in EQAS Online.

Primarily please report quantitative results. If you use different tests for quantitative and qualitative genome detection please report the results in the corresponding parameters of the entry mask.

Parameter:

- "HAV (RNA) - quantitative"
- "HAV (RNA) - qualitative"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct-/Cp-values are requested.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows:
Consider the limit of detection of your test system (e.g. 50 IU/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: **18.09.2020**

PCR/NAT - Hepatitis B Virus (361)HBV DNA *subject to RiliBAEK B 3***September 2020**

Detection of hepatitis B virus (HBV) by PCR and other nucleic acid techniques (NAT)

Instructions for test performance

Samples 361165, 361166, 361167, 361168
lyophilized plasmas (1.1 ml each)

Precautions

The plasmas are potentially positive for HBV and negative for HIV and HCV (by serology). The samples are not inactivated. All samples must be considered and treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "**Instructions for Virus Genome Detection**"
The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying the tests for the detection of HBV genome routinely used in your laboratory (even for a negative sample).

Please note! Each sample should be tested as individual sample and **not be diluted in pools**.

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The DNA of HBV should be analyzed quantitatively and/or qualitatively. Please apply your routine tests and report all necessary information according to the entry mask in EQAS Online.

Primarily please report quantitative results. If you use different tests for quantitative and qualitative genome detection please report the results in the corresponding parameters of the entry mask.

Parameter:

- "HBV (DNA) - quantitative"
- "HBV (DNA) - qualitative"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct-/Cp-values are requested.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows:
Consider the limit of detection of your test system (e.g. 50 IU/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: **18.09.2020**

PCR/NAT - (397)
HBV resistance determination
 HBV resistance *conform to RiliBAEK B 3*
September 2020

Polymerase Chain Reaction (PCR), other nucleic acid amplification techniques (NAT) and sequencing for HBV resistance determination

Instructions for test performance

Proben **397021, 397022, 397023, 397024**
Plasmid in water liquid 100µl

Information on plasmid structures are available in the electronic protocol.
 Negative samples are not supplied.

Precautions

The samples are plasmids in water with carrier DNA. The samples are negative for HIV and HCV. All samples must be treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

Plasmids can directly be applied for amplification and genotypic resistance determination of HBV (without extraction).

You receive **2 tubes** of each sample.

Test performance and submission of results

Please apply your routine tests for the amplification and genotypic resistance determination of the polymerase gene of HBV and report all necessary information according to the protocol.

10. Sequence determination of the polymerase gene for the interpretation of the genotypic resistance

Starting with the EQA term November/December 2019, reporting of your results for the sequence determination are mandatory, but are not a prerequisite for receiving a "certificate" in this EQA scheme.

Please send your sequence data as text or FASTA files stating as file name "sample number_INSTAND participant number/TN number" (e.g. 397003_TN1234) together with the Excel file.

15. Determination of the HBV genotype

Statements on the HBV genotype and genosubtype, respectively, are only requested, but are not a prerequisite for receiving a "certificate" in this EQA scheme.

20. Determination of resistance-associated mutations

The results should be reported as amino acid exchange and the position of the resistance-associated mutations (e.g. L180M). Only statements on **confirmed** resistance-associated mutations are requested. **Statements of additional mutations (e.g. polymorphisms) can be evaluated as "false"**.

The results for the determination of resistance-associated mutations will be evaluated.

30. Interpretation of genotypic resistance

Please report the interpretation of the genotypic resistance against nucleos(t)ide analoga as follows:

- susceptible (= no restricted drug efficacy)
- intermediate (= drug efficacy possibly restricted)
- resistant (= restricted drug efficacy)

Translation of your results to the selection options		
HIV-GRADE	Geno2Pheno	resistance interpretation*
resistance	resistant	resistant
possible resistance	partly resistant	intermediate
	limited susceptibility	
susceptible	susceptible	susceptible

* Only the above-mentioned results of the genotypic resistance determination will be considered for the evaluation of this EQA scheme.

Electronic protocol - submission

Please use **the electronic protocol (excel file)** for reporting your results for this EQA scheme. The electronic protocol is available for **download**:
<http://www.instand-ev.de/virus-resistance>

Please note:

State your **INSTAND participant number** in the electronic protocol.

The electronic protocol should be submitted directly to:
Heinz.Zeichhardt@iqvd.de

Deadline: **23.10.2020**

Scientific cooperation partners for this EQA scheme

Nationales Referenzzentrum für Hepatitis-B-Virus und Hepatitis-D-Virus
 Justus-Liebig-Universität Gießen
 Prof. Dr. D. Glebe, Dr. C. Schüttler,
 Dr. H. Slanina, M. Sc. F. Lehmann
 Prof. Dr. W. Gerlich, Prof. Dr. J. Ziebuhr

PCR/NAT - Hepatitis C Virus (362)HCV RNA *subject to RiliBAEK B 3***September 2020**

Detection of hepatitis C virus (HCV) by PCR and other nucleic acid techniques (NAT)

Instructions for test performance

Samples 362165, 362166, 362167, 362168
lyophilized plasmas (1.1 ml each)

Precautions

The plasmas are potentially positive for HCV and negative for HIV and HBV (by serology). The samples are not inactivated. All samples must be considered and treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "**Instructions for Virus Genome Detection**"

The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying the tests for the detection of HCV genome routinely used in your laboratory (even for a negative sample).

Please note! Each sample should be tested as individual sample and **not be diluted in pools**.

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The RNA of HCV should be analyzed quantitatively and/or qualitatively. Please apply your routine tests and report all necessary information according to the entry mask in EQAS Online.

Primarily please report quantitative results. If you use different tests for quantitative and qualitative genome detection please report the results in the corresponding parameters of the entry mask.

Parameter:

- "HCV (RNA) - quantitative"
- "HCV (RNA) - qualitative"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct-/Cp-values are requested.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows:

Consider the limit of detection of your test system (e.g. 50 IU/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under

www.instand-ev.de/en.html -> "EQAS Online"

-> "Ordering online and entering results".

Deadline: **18.09.2020**

HCV Genotyping/Subtyping (375)HCV Genotype/Subtype *subject to RiliBÄK B 3***September 2020**

Genotyping of hepatitis C virus (HCV) by PCR and other nucleic acid techniques (NAT)

Instructions for test performance

Samples 375051, 375052, 375053, 375054, 375055
lyophilized sera (1.1 ml each)

Precautions

The samples are potentially positive for HCV genome and negative for HIV and HBV (in serology), respectively. The samples are not inactivated. All samples must be treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C and +8°C) directly after receipt.

Pre-treatment of the samples

See also "**Instructions for Virus Genome Detection**"

The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying tests for genotyping of hepatitis C virus routinely used in your laboratory.

You receive **1 tube** of each sample.

PLEASE NOTE! Subtyping of Hepatitis C Virus (HCV) genotype 1 viruses required

For anti-viral treatment of infections with HCV genotype 1 with Direct Acting Agents (DAA) it will be necessary to differentiate between HCV subtypes 1a and 1b. Please see:

The updated EASL Recommendations on Treatment of Hepatitis C 2018, European Association for the Study of the Liver, Journal of Hepatology, 2018

(<https://easl.eu/wp-content/uploads/2018/10/HepC-English-report.pdf>) states: "The HCV genotype and genotype 1 subtype (1a or 1b) must be assessed prior to treatment initiation to determine the choice of therapy and its duration, among other parameters."

This is in agreement with the "S3-Leitlinie der AWMF - Prophylaxe, Diagnostik und Therapie Hepatitis-C-Virus(HCV)-Infektion", (AWMF-Registernummer 021/012)

https://www.awmf.org/uploads/tx_szleitlinien/021-012l_S3_Hepatitis-C-Virus_HCV-Infektion_2018-07.pdf

In agreement with the **Nationales Referenzzentrum für Hepatitis-C-Viren (until December 2019 Universitaetsklinikum Essen, Germany, from January 2020 Universitaetsklinikum Duesseldorf, Germany)**

we want to inform you that, starting with the EQA scheme term September 2015, it is necessary to state the HCV subtype 1a or 1b for samples containing HCV genotype 1. The differentiation between the HCV subtypes 1a and 1b is a prerequisite for the certificate of successful participation.

This means that for samples with HCV genotype 1, the exclusive statement "Genotype 1" is not sufficient for successful participation in this EQA scheme.

Test performance and result entry to EQAS Online (= "RV-Online") system

Each sample contains only one HCV genotype. Please apply the tests routinely used in your laboratory for genotyping of HCV and report all necessary information according to the protocol.

The specification of the genotype is basis for obtaining a certificate of successful participation. It is necessary for HCV genotype 1 positive samples to differentiate between subtypes 1a and 1b.

Reporting of more than one genotype for one and the same sample will not be accepted and considered as "incorrect" (except recombinants).

In case of applying different tests for genotyping/ subtyping of hepatitis C virus, please report the different methods and results separately in the corresponding categories of the protocol.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: **02.10.2020**

PCR/NAT -	(399)
HCV resistance determination	
HCV resistance	<i>conform to RiliBAEK B 3</i>
September 2020	

Polymerase Chain Reaction (PCR), other nucleic acid amplification techniques (NAT) and sequencing for HCV resistance determination

Instructions for test performance

Samples

for the HCV resistance determination of NS3 protease inhibitors and NS5A inhibitors

Sample No.	HCV resistance determination in gene region	Marix
399022	NS3	Serum
399023	NS3	Serum
399024	NS3 and NS5A	Plasma
399025	NS5A	Serum

You receive **1 tube** of each sample **with 0.5 ml sample volume**.

Negative samples are not supplied.

Precautions

All samples are positive for HCV and negative for HBV (by serology).

Statement on HIV-1:

Sample 399025 derives from a patient **co-infected with HCV and HIV** (HIV-1 viral load <50 copies / ml at the time of blood sampling).

All other above mentioned samples are negative for HIV (in serology).

The samples are not inactivated. All samples must be treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

The samples are lyophilized sera and should be reconstituted in **0.5 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature.

Test performance and submission of results

Please apply your routine tests for the extraction, amplification and resistance determination of **NS3 protease inhibitors and NS5A inhibitors, respectively**, and report all necessary information according to the protocol.

Statements on individual parameters

Parameter 10, 15, 20 and 30 for resistance testing in NS5A
Parameter 40, 45, 50 and 60 for resistance testing in NS3

10./40. Sequence determination for the interpretation of the genotypic resistance

Starting with the EQA term November/December 2019, reporting of your results for the sequence determination are mandatory, but are not a prerequisite for receiving a "certificate" in this EQA scheme.

Please send your sequence data as text or FASTA files stating as file name "sample number_INSTAND participant number/TN number" (e.g. 399003_TN1234) together with the Excel file.

15./45. Determination of the HCV geno-/subtype

Statements on the HCV genotype and subtype, respectively, are only requested, but are not a prerequisite for receiving a "certificate" in this EQA scheme.

20./50. Determination of resistance-associated mutations

The results should be reported as amino acid exchange and the position of the resistance-associated mutations (e.g. Q80K). Only statements on **confirmed** resistance-associated mutations are requested. **Statements of additional mutations (e.g. polymorphisms) can be evaluated as "false"**.

The results for the determination of resistance-associated mutations will be evaluated.

30./60. Interpretation of genotypic resistance

Please report the interpretation of the genotypic resistance against antiviral agents (direct acting agents, DAA) as follows:

- susceptible (= no restricted drug efficacy)
- intermediate (= drug efficacy possibly restricted)
- resistant (= restricted drug efficacy)

The results for the interpretation of the genotypic resistance will be evaluated.

Electronic protocol - submission

Please use **the electronic protocol (excel file)** for reporting your results for this EQA scheme. The electronic protocol is available for **download**:

<http://www.instand-ev.de/virus-resistance>

Please note:

State your **INSTAND participant number** in the electronic protocol.

The electronic protocol should be submitted directly to:

Heinz.Zeichhardt@iqvd.de

Deadline: **23.10.2020**

Scientific cooperation partners for this EQA scheme

Nationales Referenzzentrum für Hepatitis-C-Viren
Universitätsklinikum Düsseldorf
Institut für Virologie
Prof. Dr. J. Timm
Prof. Dr. O. Adams
Dr. N. Lübke

Universität Duisburg-Essen
Universitätsklinikum Essen
Prof. Dr. U. Dittmer
Prof. Dr. S. Ross

PCR/NAT - Hepatitis D Virus (400)

HDV RNA

conform to RiliBÄK B 3

September 2020

Detection of hepatitis D virus (HDV) by PCR and other nucleic acid techniques (NAT)

Instructions for test performance

Samples **400045, 400046, 400047, 400048**
lyophilized plasmas (1.1 ml each)

Precautions

The plasmas are potentially positive for HBV/HDV and negative for HIV and HCV (in serology). The samples are not inactivated. All samples must be considered and treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "**Instructions for Virus Genome Detection**"

The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying the tests for the detection of HDV genome routinely used in your laboratory (even for a negative sample).

Please note! Each sample should be tested as individual sample and **not be diluted in pools**.

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The RNA of HDV should be analyzed quantitatively and/or qualitatively. Please apply your routine tests and report all necessary information according to the entry mask in EQAS Online.

If you use different tests for quantitative and qualitative genome detection please report the results in the corresponding parameters of the entry mask.

Please do not report a qualitative interpretation from a quantitative PCR/NAT result.

Parameter:

- "HDV (RNA) - quantitative"
- "HDV (RNA) - qualitative"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct-/Cp-values are requested.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows: Consider the limit of detection of your test system (e.g. 50 copies/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: **18.09.2020**

PCR/NAT - Hepatitis E Virus (380)
HEV RNA *subject to RiliBAEK B 3 (as of RiliBAEK 2019)*
September 2020

Detection of hepatitis E virus (HEV) by PCR and other nucleic acid techniques (NAT)

Instructions for test performance

Samples **380073 (lyophil. suspension of feces)**
380074, 380075, 380076 (lyophil. plasmas)
(1.1 ml each)

Precautions

The samples are potentially positive for HEV. The plasma samples consist of plasma (negative by serology for HIV, HBV and HCV) spiked either with plasmids (contain subgenomic HEV DNA) or with cleared suspension of HEV positive feces. All suspensions of feces are not tested for HIV, HBV and HCV. The samples are not inactivated. All samples must be considered and treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "**Instructions for Virus Genome Detection**"
The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently, please analyze the samples as native specimens applying the tests for the detection of HEV genome routinely used in your laboratory (even for a negative sample).

Please note! Each sample should be tested as individual sample and **not be diluted in pools**.

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The RNA of HEV should be analyzed quantitatively and/or qualitatively. Please apply your routine tests and report all necessary information according to the entry mask in EQAS Online. Primarily, please report qualitative results. If you use different tests for quantitative and qualitative genome detection, please report the results in the corresponding parameters of the entry mask.

Parameter:

- "HEV (RNA) - quantitative"
- "HEV (RNA) - qualitative"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct/Cp-values are requested.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows:
Consider the limit of detection of your test system (e.g. 50 copies/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: **18.09.2020**

PCR/NAT - HIV-1 (RNA) (360)
HIV-1 RNA *subject to RiliBAEK B 3*
September 2020

Detection of HIV-1 by PCR and other nucleic acid techniques (NAT)

Instructions for test performance

Samples **360165, 360166, 360167, 360168**
lyophilized plasmas (1.1 ml each)

Precautions

The samples contain plasmas negative for HIV, HBV and HCV (by serology) which were spiked with cell culture propagated HIV-1 (virus heat inactivated). All plasmas must be considered and treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "**Instructions for Virus Genome Detection**"
The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying the tests for the detection of HIV-1 genome routinely used in your laboratory (even for a negative sample).

Please note! Each sample should be tested as individual sample and **not be diluted in pools**.

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The RNA of HIV-1 should be analyzed quantitatively and/or qualitatively. Please apply your routine tests and report all necessary information according to the entry mask in EQAS Online.

Primarily please report quantitative results. If you use different tests for quantitative and qualitative genome detection please report the results in the corresponding parameters of the entry mask.

Parameter:

- "HIV-1 (RNA) - quantitative"
- "HIV-1 (RNA) - qualitative"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct/Cp-values are requested.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows:
Consider the limit of detection of your test system (e.g. 50 copies/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: **18.09.2020**

PCR/NAT - (383)
HIV-1 drug resistance determination
Standard program for protease inhibitors and reverse transcriptase inhibitors
HIV-1 drug resistance conform to RiliBAEK B 3
September 2020

Polymerase Chain Reaction (PCR), other nucleic acid techniques (NAT) and sequencing for HIV-1 drug resistance determination of protease inhibitors and reverse transcriptase inhibitors

Instructions for test performance

Samples: **383027, 383028, 383029, 383030**
Virus (inactivated) in plasma
liquid 1100 µl

The sample set may comprise "educational" samples. Neagive samples are not included.

Precautions

The samples are plasmids in water with carrier DNA or plasmas (spiked with inactivated HIV-1 from cell culture supernatants), respectively. The plasmas used for spiking are each negative for HIV, HBV and HCV (by serology). All samples must be considered and treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples for amplification

Virus (inactivated) in plasma liquid 1100 µl

The liquid samples can be used for nucleic acid extraction without further pre-preparation. Subsequently please analyze the samples applying the methods for amplification and HIV-1 genotypic drug resistance determination routinely used in your laboratory.

You receive **2 tubes** of each sample.

Test performance - amplification - genotypic drug resistance determination

Please apply your routine tests for amplification and genotypic HIV-1 drug resistance determination of protease inhibitors and reverse transcriptase inhibitors.

Instructions for reporting results

For reporting your results, please follow the instructions on the HIV-GRADE-homepage / section "EQA Ringversuche" (see below: Submission of results). The following informations are requested:

• **Applied methods**

Specify the applied methods for extration, amplification and sequencing for each analyzed sample.

• **Applied algorithms**

Specify the applied algorithms used for analysis of the sequences (mutation identification and genotypic drug resistance determination).

• **Sequence data of the whole resistance related sequence range for**

- the protease range and (*amino acid range 10-90*) and
- the reverse transcriptase range (*amino acid range 41-238*).

Please note: Your reported sequence data should completely include the above-mentioned resistance related sequence ranges.

• **HIV-1 Subtype analysis**

Report the HIV-1 subtype in section *Sequence Information*.

• **Interpretation of resistance / sensitivity to antiretroviral drugs (Estimation of susceptibility according S/I/R-scheme)**

For receiving a certificate of successful participation of this EQA-scheme, it is necessary to interpret the sequence data for resistance / susceptibility to antiretroviral drugs according to the **3-level S/I/R scheme**, as agreed with the scientific cooperation partners.

For translation of sensitivity estimations based on other **interpretation algorithms (ANRS, HIVdb, REGA)**,

please see also: homepage "Stanford University, HIV Drug Resistance Database", section „Algorithms“, <https://hivdb.stanford.edu/page/release-notes/>

Please state your susceptibility estimation for all indicated drugs even if they are no longer used for standard therapy according to the local therapy recommendations.

The following interpretation algorithms are used for the evaluation: Stanford HIVdb, REGA algorithm, ANRS and HIV-GRADE. The evaluation will be based on the overall consensus of these interpretation algorithms (examples see table 1).

Table 1: Examples of accepted interpretations depending on the susceptibility estimation by different algorithms

drug	interpretation scheme				accepted interpretation(s)
	Stanford HIVdb	REGA	ANRS	HIV-GRADE	
A	S	S	S	S	S
B	I	I	I	I	I
C	R	R	R	R	R
D	S	I	S	I	S and I (*)
E	R	I	I	I	I and R (*)

(*) In case of deviating interpretations by the algorithms, all listed interpretations are accepted

Electronic result submission with HIV-GRADE

Please report your results for this EQA scheme via the **HIV-GRADE web portal**. The Link to the HIV-GRADE web portal is available on the INSTAND homepage: <http://www.instand-ev.de/virus-resistance>

Your personal access:

eMail-address:

Please use your INSTAND registration email address.

Participant-Number:

Please use your INSTAND participant number.

Homepage
HIV-1 Tool
HIV2EU Tool
HBV Tool
Explanations
Downloads
EQA - Ringversuche
About GRADE
LOGIN

Eingabebformular INSTAND Ringversuch

Der HIV-GRADE e.V. freut sich den INSTAND e.V. bei der Datenerfassung für die Ringversuche RV Virologie 383 - 384 (2015/2016) unterstützen zu können. Nach Verteilung der Ringversuchsproben besteht für die Teilnehmer die Möglichkeit sich hier zum [Eingabebformular](#) weiterleiten zu lassen.

INSTAND e.V. ist der wichtigste Anbieter für externe Qualitätssicherung in Deutschland und bietet eine große Palette an Ringversuchen aus allen Bereichen der medizinischen Diagnostik an.

The HIV-GRADE society is honored to support the INSTAND e.V. in collecting the data for the EQA Schemes 383 - 384 (2015/2016). After the distribution of the samples to the participants the link to the appropriate [form for data entry](#) will be provided.

INSTAND e.V. is the most important provider for external quality assessment in Germany with programs in all fields of medical diagnostics.

PCR/NAT - (384)
HIV-1 drug resistance determination
Additional program for integrase inhibitors
and determination of tropism
HIV-1 drug resistance *conform to RiliBAEK B 3*
September 2020

Polymerase Chain Reaction (PCR), other nucleic acid techniques (NAT) and sequencing for HIV-1 drug resistance determination of integrase inhibitors and determination of tropism

Instructions for test performance

Samples

[Virus \(inactivated\) in plasma](#) [liquid](#) [1100 µl](#)
384015 sample for drug resistance determination of integrase inhibitors
384016 sample for determination of tropism

Neagive samples are not included.

Precautions

The samples are plasmas (spiked with inactivated HIV-1 from cell culture supernatants). The plasmas used for spiking are each negative for HIV, HBV and HCV (by serology). All samples must be considered and treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples for amplification

[Virus \(inactivated\) in plasma](#) [liquid](#) [1100 µl](#)
The liquid samples can be used for nucleic acid extraction without further pre-preparation. Subsequently please analyze the samples applying the methods for amplification and HIV-1 genotypic drug resistance determination and determination of tropism routinely used in your laboratory.

You receive **2 tubes** of each sample.

Test performance - amplification - genotypic drug resistance determination and determination of tropism

Please apply your routine tests for amplification and HIV-1 genotypic drug resistance determination or determination of tropism, respectively.

Instructions for reporting results

For reporting your results, please follow the instructions on the HIV-GRADE-homepage / section "EQA Ringversuche" (see below: Submission of results). The following informations are requested:

Deadline: 23.10.2020

Scientific cooperation partners for this EQA scheme

Ludwig-Maximilians-Universität München,
Max-von-Pettenkofer Institut, Klinische Virologie,
Nationales Referenzzentrum für Retroviren
Prof. Dr. O. T. Keppler, Prof. Dr. J. Eberle,
Prof. Dr. L. Gürtler, Dr. Hans Nitschko

Friedrich-Alexander-Universität Erlangen-Nürnberg,
Universitätsklinikum Erlangen, Institut für Klinische und
Molekulare Virologie
Prof. Dr. K. Überla, Dr. K. Korn

IMD Medizinisches Versorgungszentrum, Frankfurt
PD Dr. M. Stürmer

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Prof. Dr. A. Berger

Acknowledgement

We thank HIV-GRADE e.V., especially Dr. M. Obermeier and M. Schütze, for implementation of the special link on the HIV-GRADE homepage for the INSTAND EQA schemes (383) and (384).

Drug resistance determination of integrase inhibitors

• Applied methods

Specify the applied methods for extraction, amplification and sequencing for each analyzed sample.

• Applied algorithms

Specify the applied algorithms used for analysis of the sequences (mutation identification and genotypic drug resistance determination).

• Sequence data of the whole resistance related sequence range for

- the integrase range
(*amino acid range 49-263*)

- Please note: Your reported sequence data should completely include the above-mentioned resistance related sequence range.

• HIV-1 Subtype analysis

Report the HIV-1 subtype in section *Sequence Information*.

• Interpretation of resistance / sensitivity to antiretroviral drugs (Estimation of susceptibility according S/I/R-scheme)

For receiving a certificate of successful participation of this EQA-scheme, it is necessary to interpret the sequence data for resistance / susceptibility to antiretroviral drugs according to the **3-level S/I/R scheme**, as agreed with the scientific cooperation partners.

For translation of sensitivity estimations based on other interpretation algorithms (ANRS, HIVdb, REGA), please see also: homepage "Stanford University, HIV Drug Resistance Database" Release Notes HIVdb version 8.8 (13.02.2019), *section „Algorithms“*, <https://hivdb.stanford.edu/page/release-notes/>

Please state your susceptibility estimation for all indicated drugs even if they are no longer used for standard therapy according to the local therapy recommendations.

The following interpretation algorithms are used for the evaluation: Stanford HIVdb, REGA algorithm, ANRS and HIV-GRADE. The evaluation will be based on the overall consensus of these interpretation algorithms (examples see table 1).

Table 1: Examples of accepted interpretations depending on the susceptibility estimation by different algorithms

drug	interpretation scheme				accepted interpretation(s)
	Stanford HIVdb	REGA	ANRS	HIV-GRADE	
A	S	S	S	S	S
B	I	I	I	I	I
C	R	R	R	R	R
D	S	I	S	I	S and I (*)
E	R	I	I	I	I and R (*)

(*) In case of deviating interpretations by the algorithms, all listed interpretations are accepted

Determination of genotypic Tropism

• Applied methods

Specify the applied methods for extraction, amplification and sequencing for each analyzed sample.

• Applied algorithms

Specify the applied algorithms used for analysis of the sequences (tropism determination).

• Sequence data of the whole tropism related sequence range for

- the gp120 range

Please note: The reported sequence data should include all tropism related sequence ranges.

• HIV-1 subtype analysis

Report the HIV-1 subtype in section *Sequence Information*.

• Statement of the interpreted tropism

Please state the determined tropism (e.g. CXCR4).

Electronic result submission with HIV-GRADE

Please report your results for this EQA scheme via the **HIV-GRADE web portal**. The Link to the HIV-GRADE web portal is available on the INSTAND homepage: <http://www.instand-ev.de/virus-resistance>

Your personal access:

eMail-address:

Please use your INSTAND registration email address

Participant-Number:

Please use your INSTAND participant number



Homepage
HIV-1 Tool
HIV2EU Tool
HBV Tool
Explanations
Downloads
EQA - Ringversuche
About GRADE
LOGIN

Eingabebformular INSTAND Ringversuch

Der HIV-GRADE e.V. freut sich den INSTAND e.V. bei der Datenerfassung für die Ringversuche RV Virologie 383 - 384 (2015/2016) unterstützen zu können. Nach Verteilung der Ringversuchsproben besteht für die Teilnehmer die Möglichkeit sich hier zum [Eingabebformular](#) weiterleiten zu lassen.

*INSTAND e.V. ist der wichtigste Anbieter für externe Qualitätssicherung in Deutschland und bietet eine große Palette an Ringversuchen aus allen Bereichen der medizinischen Diagnostik an

The HIV-GRADE society is honored to support the INSTAND e.V in collecting the data for the EQA Schemes 383 - 384 (2015/2016). After the distribution of the samples to the participants the link to the appropriate [form for data entry](#) will be provided.

*INSTAND e.V. is the most important provider for external quality assessment in Germany with programs in all fields of medical diagnostics.

Deadline:

23.10.2020

Scientific cooperation partners for this EQA scheme

Ludwig-Maximilians-Universität München,
Max-von-Pettenkofer Institut, Klinische Virologie,
Nationales Referenzzentrum für Retroviren
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Prof. Dr. L. Gürtler, Dr. Hans Nitschko

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Prof. Dr. A. Berger

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PCR/NAT -	(405)
Human Herpesvirus 6 (HHV-6)	
HHV-6 DNA	<i>conform to RiliBÄK B 3</i>
September 2020	

Detection of human herpesvirus 6 (HHV-6) by PCR and other nucleic acid techniques (NAT)

Instructions for test performance

Samples **405005, 405006, 405007, 405008**
lyophilized cell lysates (1.1 ml each)

Precautions

The samples are potentially positive for HHV-6 and negative for HIV, HBV and HCV. The samples are not inactivated. All samples must be considered and treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "**Instructions for Virus Genome Detection**"
The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying the tests for the detection of HHV-6 routinely used in your laboratory (even for a negative sample).

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The DNA of HHV-6 should be analyzed quantitatively and/or qualitatively. Please apply your routine tests and report all necessary information according to the entry mask.

If you use different tests for quantitative and qualitative genome detection, please report the results in the corresponding parameters of the entry mask as indicated. Please do not report a qualitative interpretation from a quantitative PCR/NAT result.

Parameter:

- "HHV-6 (DNA) - quantitative"
- "HHV-6 (DNA) - qualitative"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct-/Cp-values are requested.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows:
Consider the limit of detection of your test system (e.g. 50 copies/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: **18.09.2020**

PCR/NAT - JC Virus (394)
JC Virus DNA *conform to RiliBÄK B 3*
September 2020

Detection of JC virus by PCR and other nucleic acid techniques (NAT)

Instructions for test performance

Samples 394045, 394046, 394047, 394048
lyophilized suspensions of urine
(1.1 ml each)

Precautions

The suspensions of urine are potentially positive for JC virus, BK virus and CMV and not tested for HIV, HBV and HCV genomes, respectively. The samples are not inactivated. All samples must be considered and treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "**Instructions for Virus Genome Detection**"
The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying the tests for the detection of JC virus genome routinely used in your laboratory (even for a negative sample).

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The DNA of JC virus should be analyzed quantitatively and/or qualitatively. Please apply your routine tests and report all necessary information according to the entry mask.

If you use different tests for quantitative and qualitative genome detection, please report the results in the corresponding parameters of the entry mask as indicated. Please do not report a qualitative interpretation from a quantitative PCR/NAT result.

Parameter:

- "JC virus (DNA) - quantitative"
- "JC virus (DNA) - qualitative"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct-/Cp-values are requested.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows:
Consider the limit of detection of your test system (e.g. 50 IU/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: 18.09.2020

PCR/NAT - Parainfluenza Viruses (388)
PIV RNA *conform to RiliBÄK B 3*
September 2020

Detection of parainfluenza viruses by PCR and other nucleic acid techniques (NAT) with the option of typing

Instructions for test performance

Samples 388053, 388054, 388055, 388056
lyophilized cell lysates (1.1 ml each)

Precautions

The samples are potentially positive for parainfluenza viruses and negative for HIV, HBV and HCV. The samples are not inactivated. All samples must be treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "**Instructions for Virus Genome Detection**"
The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying your routine tests for the detection of parainfluenza virus genome (even for a negative sample). In case of positive samples please determine the parainfluenza subtype.

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The RNA of parainfluenza viruses should be analyzed quantitatively and/or qualitatively. In addition please determine the parainfluenza subtype. Please apply your routine tests and report all necessary information according to the entry mask.

Primarily please report qualitative results. Please do not report a qualitative interpretation from a quantitative PCR/NAT result.

Parameter:

- "Parainfluenza viruses (RNA) - quantitative"
- "Parainfluenza viruses (RNA) - qualitative"
- "Parainfluenza viruses (RNA) - type identification"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct-/Cp-values are requested.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows:
Consider the limit of detection of your test system (e.g. 50 copies/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: 18.09.2020

PCR/NAT - Parechovirus (407)
HPeV RNA *conform to RiliBÄK B 3*
September 2020

Detection of parechovirus by PCR and other nucleic acid techniques (NAT)

Instructions for test performance

Samples 407005, 407006, 407007, 407008
lyophilized cell lysates (1.1 ml each)

Precautions

The samples are potentially positive for parechovirus and negative for HIV, HBV and HCV. The samples are not inactivated. All samples must be considered and treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "**Instructions for Virus Genome Detection**"
The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying the tests for the detection of parechovirus routinely used in your laboratory (even for a negative sample).

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The RNA of parechovirus should be analyzed quantitatively and/or qualitatively. Please apply your routine tests and report all necessary information according to the entry mask.

If you use different tests for quantitative and qualitative genome detection, please report the results in the corresponding parameters of the entry mask as indicated. Please do not report a qualitative interpretation from a quantitative PCR/NAT result.

Parameter:

- "Parechovirus (RNA) - quantitative"
- "Parechovirus (RNA) - qualitative"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct/Cp-values are requested.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows:
Consider the limit of detection of your test system (e.g. 50 copies/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: 18.09.2020

PCR/NAT - Parvovirus B19 (367)
Parvo B19 DNA *subject to RiliBAEK B 3*
September 2020

Detection of parvovirus B19 by PCR and other nucleic acid techniques (NAT)

Instructions for test performance

Samples 367165, 367166, 367167, 367168
lyophilized plasmas (1.1 ml each)

Precautions

The samples are potentially positive for parvovirus B19 and negative for HIV, HBV and HCV (by serology). The samples are not inactivated. All samples must be treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "**Instructions for Virus Genome Detection**"
The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying your routine tests for the detection of parvovirus B19 genome (even for a negative sample).
Please note! Each sample should be tested as individual sample and **not be diluted in pools**.

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The DNA of parvovirus B19 should be analyzed quantitatively and/or qualitatively. Please apply your routine tests and report all necessary information according to the entry mask in EQAS Online. Primarily please report quantitative results. If you use different tests for quantitative and qualitative genome detection please report the results in the corresponding parameters of the entry mask.

Parameter:

- "Parvovirus B19 (DNA) - quantitative"
- "Parvovirus B19 (DNA) - qualitative"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct/Cp-values are requested.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows:
Consider the limit of detection of your test system (e.g. 50 IU/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: 18.09.2020

PCR/NAT - Rabies Virus (390)
RABV RNA conform to RiliBÄK B 3
September 2020

Detection of rabies virus (RABV) by PCR and other nucleic acid techniques (NAT)

Instructions for test performance

Samples 390025, 390026, 390027, 390028
lyophilized rabies vaccine, inactivated
(1.1 ml each)

Precautions

The samples are potentially positive for genome of rabies virus (**rabies vaccine; inactivated**) and negative for HIV, HBV and HCV, respectively. All samples must be treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "**Instructions for Virus Genome Detection**"
The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying the tests for the detection of RABV genome routinely used in your laboratory (even for a negative sample).

Please note! Each sample should be tested as individual sample and **not be diluted in pools**.

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The RNA of RABV should be analyzed qualitatively. Please apply your routine tests and report all necessary information according to the entry mask. If you use different tests for qualitative genome detection please report the results in the corresponding parameters of the entry mask.

Parameter:

- "Rabies virus (RNA) - qualitative"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct-/Cp-values are requested.

Please enter your **EQAS results** on the INSTAND website under

www.instand-ev.de/en.html -> "EQAS Online"
-> "Ordering online and entering results".

Deadline: **18.09.2020**

PCR/NAT – Torque Teno Virus (408)
TTV DNA conform to RiliBÄK B 3
September 2020 NEW

Detection of Torque Teno virus (TTV) by PCR and other nucleic acid techniques (NAT)

Instructions for test performance

Samples 408001, 408002, 408003, 408004
lyophilized plasmas (1.1 ml each)

Precautions

The samples are potentially positive for TTV and consist of plasma (negative for HIV, HBV and HCV in serology) spiked with TTV positive urine suspensions. The urine suspensions were not tested for HIV, HBV and HCV. All samples are not inactivated must be treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "**Instructions for Virus Genome Detection**"
The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying the tests for the detection of TTV genome routinely used in your laboratory.

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The DNA of TTV should be analyzed quantitatively and/or qualitatively. Please apply your routine tests and report all necessary information according to the entry mask.

Primarily please report qualitative results. If you use different tests for quantitative and qualitative genome detection please report the results in the corresponding parameters of the entry mask.

Parameter:

- "Torque Teno virus (DNA) - quantitative"
- "Torque Teno virus (DNA) - qualitative"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct-/Cp-values are requested.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows: Consider the limit of detection of your test system (e.g. 50 copies/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please enter your **EQAS results** on the INSTAND website under

www.instand-ev.de/en.html -> "EQAS Online"
-> "Ordering online and entering results".

Deadline: **18.09.2020**

PCR/NAT - West Nile virus (391)WNV RNA *subject to RiliBAEK B 3 (as of RiliBAEK 2019)***September 2020**

Detection of West Nile viruses (WNV) by PCR and other nucleic acid techniques (NAT) with the option of lineage identification.

Instructions for test performance

Samples 391095, 391096, 391097, 391098, 391099, 391100
lyophilized plasmas (1.1 ml each)

Precautions

The samples contain human plasmas (spiked with heat-inactivated West Nile viruses from cell culture). The plasmas are negative for HIV, HBV and HCV (by serology), respectively. All samples must be considered and treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "**Instructions for Virus Genome Detection**"
The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying your routine tests for the detection of West Nile virus genome (even for a negative sample). In case of positive samples please determine the West Nile virus lineage.

You receive **2 tubes** of each sample.

Test performance and result entry to EQAS Online (= "RV-Online") system

The RNA of West Nile virus should be analyzed quantitatively and/or qualitatively. In addition, please determine the West Nile virus lineage. Please apply your routine tests and report all necessary information according to the entry mask in EQAS Online. Primarily please report qualitative results. If you use different tests for quantitative and qualitative genome detection please report the results in the corresponding parameters of the entry mask.

Parameter:

- "WNV (RNA) - quantitative"
- "WNV (RNA) - qualitative"
- "WNV (RNA) - lineage identification"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct-/Cp-values are requested.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows: Consider the limit of detection of your test system (e.g. 50 copies/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: 18.09.2020

PCR/NAT - Zika virus (403)ZIKV RNA *conform to RiliBÄK B 3***September 2020**

Detection of Zika virus (ZIKV) by PCR and other nucleic acid techniques (NAT) with the option of lineage identification.

Instructions for test performance

Samples 403037, 403038, 403039, 403040
lyophilized plasmas (1.1 ml each)

Precautions

The samples contain human plasmas (spiked with heat-inactivated Zika viruses from cell culture). The plasmas are negative for HIV, HBV and HCV in serology). All samples must be considered and treated as potentially infectious materials and must be used only for diagnostic purpose following adequate precautions.

Storage of samples

The samples have to be stored in a refrigerator (+2°C to +8°C) directly after receipt.

Pre-treatment of the samples

See also "**Instructions for Virus Genome Detection**"
The samples should be reconstituted in **1.1 ml aqua bidest. (sterile, pyrogen-free, PCR-grade)** directly before testing. The samples should be reconstituted by vigorous mixing (Vortex) for 20 min at room temperature. Subsequently please analyze the samples as native specimens applying your routine tests for the detection of Zika virus genome. In case of positive samples please determine the Zika virus lineage.

You receive **2 tubes** of each sample.

Test performance

The RNA of Zika virus should be analyzed quantitatively and/or qualitatively. In addition, please determine the Zika virus lineage. Please apply your routine tests and report all necessary information according to the entry mask in EQAS Online.

If you use different tests for quantitative and qualitative genome detection please report the results in the corresponding parameters of the entry mask.

Please do not report a qualitative interpretation from a quantitative PCR/NAT result.

Parameter:

- "Zika virus (RNA) - quantitative"
- "Zika virus (RNA) - qualitative"
- "Zika virus (RNA) - lineage identification"

All results should be reported according to the requests of the entry mask in EQAS Online. Ct-/Cp-values are requested.

Please note:

If your test system reports "below level of detection" as quantitative result, please proceed as follows: Consider the limit of detection of your test system (e.g. 50 copies/ml) and enter under "Result (quant)" the result "< 50" for the corresponding sample.

Please enter your **EQAS results** in the EQAS Online system on the INSTAND website under www.instand-ev.de/en.html -> "EQAS Online" -> "Ordering online and entering results".

Deadline: 18.09.2020

INSTAND Expert Laboratories for EQASs in Virus Diagnostics

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