DRG:HYBRiD•XL®

Instructions for Use

Salivary Cortisol

IVD

CE

REF **HYE-5344**

Σ **40 tests**

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ASSAY PROTOCOL BARCODE (APB)

(Version 2.61 Software or later / ab Softwareversion 2.61 oder höher / Versione Software 2.61 o superiore / Versión de Software 2.61 o posterior / Version de logiciel 2.61 et supérieure / Wersja oprogramowania 2.61 lub późniejsza)

HYE-5344 – v2.61.1

The barcode must be used to install the assay protocol into the DRG:HYBRiD-XL software via the SCAN NEW LOT page.

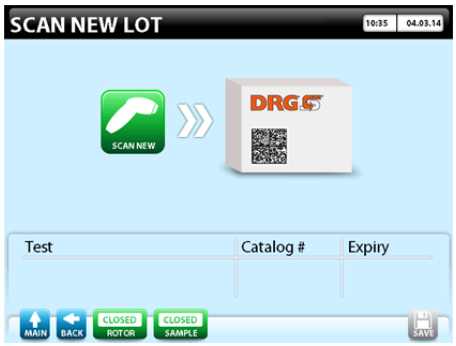
Der Barcode muss in dem Menü „NEUES LOT SCANNEN“ eingelesen werden, um das Protokoll in der DRG:HYBRiD-XL-Software zu installieren.

Il codice a barre deve essere utilizzato per installare il protocollo del assay nel software DRG:Hybrid-XL tramite la pagina SCAN NUOVO LOTTO.

El código de barras debe utilizarse para instalar el protocolo de ensayo en el software del DRG:HYBRiD-XL a través del menú SCAN NEW LOT.

Le code barre doit être lu dans le menu SCAN NOUVEAU LOT afin d´installer le protocole DRG:HYBRiD-XL Software.

Kod kreskowy powinien być uzyty do instalacji protokołu oznaczenia w analizatorze DRG:HYBRiD-XL w zakładce SKANUJ NOWY LOT



Please refer to section **3**: **Routine Procedures: “Installing a new assay product”** of the User Manual v2.60 or later.

Bitte lesen Sie dazu auch Abschnitt **3 Routineprozeduren: “Installation eines neuen Assays/eines neuen Assay-Protokolls“** im Benutzerhandbuch v2.60 oder höher.

Si prega di fare riferimento alla sezione **3: Procedure ordinarie: "Installazione di un nuovo Assay"** del Manuale utente v2.60 o superiore.

Consulte la sección **3 Procesos Rutinarios: "Instalación de un nuevo ensayo"** en el Manual del usuario v2.60 o posterior.

Merci de vous référer au chapitre **3 : Procédure de routine: " Installation d´un nouvel assay/ un nouveau protocole d´assay"** dans le manuel d´utilisation à partir de la version v2.60.

Proszę zapoznać się z sekcją **3: Prcedury rutynowe: "Instalowanie nowego oznaczenia"** w Instrukcji Użytkownika, wersja 2.60 lub późniejsza

Contents

1 INTRODUCTION

1.1 Intended Use

The **DRG:HYBRiD-XL Salivary Cortisol** is an enzyme immunoassay for the quantitative *in vitro diagnostic* measurement of cortisol in saliva.

Only for use with the DRG:HYBRiD-XL Analyzer.

1.2 Summary and Explanation

Cortisol, the most potent glucocorticoid, is produced by the zona fasciculate of the human adrenal cortex (1-3). It is synthesized from cholesterol and its production is stimulated by pituitary adrenocorticotropic hormone (ACTH) in response to corticotropin-releasing hormone (CRH). ACTH and CRH secretions are inhibited by high cortisol levels in a negative feedback loop. Cortisol acts through specific intracellular receptors and affects numerous physiologic systems including immune function, glucose counter regulation, vascular tone, and bone metabolism.

Cortisol release follows a diurnal rhythm with highest concentrations in the morning (about 1 hour after wakening). Thereafter, Cortisol concentration steadily decreases to a very low level 12 hours later (4-7). Cortisol secretion increases in response to any stress in the body, whether physical (such as illness, trauma, surgery, or temperature extremes) or psychological (8-14). After secretion, cortisol causes a breakdown of muscle protein, leading to release of amino acids into the bloodstream. These amino acids are then used by the liver to synthesize glucose for the brain, a process called gluconeogenesis. Cortisol also leads to the release of fatty acids from fat cells and its utilization in muscle cells. Taken together, these energy-directing processes prepare the individual to deal with stressors and ensure that the brain receives adequate energy sources.

Elevated cortisol levels and lack of diurnal variation have been identified with Cushing's disease (ACTH hypersecretion) (7). CRH is released in a cyclic fashion by the hypothalamus, resulting in diurnal peaks (elevated in the morning) and nadirs (low in the evening) for plasma ACTH and cortisol levels. The diurnal variation is lost in patients with Cushing and these patients have elevated levels of evening plasma cortisol. The measurement of late-night salivary cortisol is an effective and convenient screening test for Cushing syndrome (15). Elevated circulating cortisol levels have also been identified in patients with adrenal tumors (16). Low cortisol levels are found in primary adrenal insufficiency (e.g. adrenal hypoplasia, Addison's disease) and in ACTH deficiency (17). Due to the normal circadian variation in cortisol levels, distinguishing normal from abnormally low cortisol levels can be difficult, therefore several daily collections are recommended.

Saliva is an excellent medium to measure steroids because it is a natural ultra-filtrate of blood. 90-99% of steroid hormones in the blood are bound to carrier proteins (corticoid-binding globulin, sex-hormone binding globulin and albumin) and are unavailable to target tissues. Only about 1-10% of the steroids in blood are in the unbound or free fraction, and can diffuse into target tissues of the body and into saliva. The process of passive diffusion of non-bound steroid hormones is supported by their low molecular weight (less than 400 daltons) and relative lipophilicity, thus enabling them to freely diffuse from blood to saliva (18-21).

2 PRINCIPLE OF THE TEST

The DRG:HYBRiD-XL Salivary Cortisol Kit is a solid phase enzyme-linked immunosorbent assay (ELISA) based on the **principle of competitive binding.**

The antibody coated wells (ACW) of the reagent cartridges are coated with a monoclonal (mouse) antibody directed towards a unique antigenic site of the cortisol molecule. Endogenous cortisol of a patient sample competes with a cortisol-horseradish peroxidase conjugate for binding to the coated antibody. After incubation the unbound conjugate is washed off.

The amount of bound peroxidase conjugate is inversely proportional to the concentration of cortisol in the sample.

Having added the substrate solution, the intensity of colour developed is inversely proportional to the concentration of cortisol in the patient sample.

3 WARNINGS AND PRECAUTIONS

1. This kit is for in vitro diagnostic use only.
   For professional use only.
2. This kit can only be used in combination with the DRG:HYBRiD-XL Analyzer
3. Before starting the assay, read the instructions completely and carefully. Use the valid version of the package insert provided with the kit. Be sure that everything is clear and understood.
4. **Do not remove, exchange, discard or damage any of the barcode labels provided with each kit and its components. All barcodes build an integral system for the kit lot.**
5. Respect the general safety measures for use of laboratory reagents.
6. All reagents of this test kit which contain human serum or plasma have been tested and confirmed negative for HIV I/II, HBsAg and HCV by FDA approved procedures. All reagents, however, should be treated as potential biohazards in use and for disposal.
7. Never pipet by mouth and avoid contact of reagents and specimens with skin and mucous membranes.
8. Do not smoke, eat, drink or apply cosmetics in areas where specimens or kit reagents are handled.
9. Wear appropriate disposable gloves when handling specimens and reagents. Microbial contamination of reagents or specimens may cause false results.
10. Handling should be done in accordance with the procedures defined by an appropriate national biohazard safety guideline or regulation.
11. Do not use reagents beyond expiry date as shown on the kit labels.
12. Unused reagent cartridges must be stored at 2 °C to 8 °C in the sealed foil pouch with desiccant provided.
13. Optimal test results are only obtained when using calibrated pipettes.
14. Do not mix or use components from kits with different lot numbers. It is advised not to interchange reagent cartridges of different kits even of the same lot. The kits may have been shipped or stored under different conditions and the binding characteristics of the wells in the reagent cartridges may differ slightly.
15. Some reagents contain Proclin 300, BND and/or MIT as preservatives. In case of contact with eyes or skin, flush immediately with water.
16. TMB substrate has an irritant effect on skin and mucosa. In case of possible contact, wash eyes with an abundant amount of water and skin with soap and plenty of water. Wash contaminated objects before reusing them. If inhaled, take the person to open air.
17. Chemicals and prepared or used reagents have to be treated as hazardous waste according to the national biohazard safety guidelines or regulations.
18. For information on hazardous substances included in the kit please refer to Safety Data Sheets.
    For professional users the Safety Data Sheet for this product is available upon request directly from DRG.

4 REAGENTS

4.1 Reagents provided

4.1.1 Reagent Cartridges

40 pieces containing the following:

- ***Antibody Coated Well (ACW)***
  coated with anti-cortisol antibody (monoclonal).
- ***Enzyme Conjugate***, 170 µL,
  cortisol antigen conjugated with horseradish peroxidase;
  Contains non-mercury preservative.
- ***Substrate Solution***, 270 µL
  Tetramethylbenzidine (TMB).

4.1.2 Re-Calibrator 1 & 2

2 vials, 1 mL each, ready to use;

For re-calibration of the quantitative DRG:HYBRiD-XL Salivary Cortisol test.

Concentrations are lot-specific.

Conversion: 1 ng/mL = 2.76 nmol/L

Re-Calibrators are standardised against the following reference material: C-106 (Cerilliant)

Contain non-mercury preservative.

4.1.3 Control 1 & 2

2 vials, 1 mL each, ready to use;

For control values and ranges please refer to the bar code on vial label or to the QC-Datasheet.

Contain non-mercury preservative.

4.2 Materials required but not provided

- General needed laboratory equipment
- Ultra-pure water
  DRG recommends to use Clinical Laboratory Reagent Water (CLRW) according to CLSI guideline 3C-A4 with the following specifications:
  Resistivity at 25 °C [MΩ·cm]: > 10
  Conductivity at 25 °C [µS·cm^{-1}]: < 0.1
  Total Organic Carbon/p.p.b.[µg/L] : < 50
  Colloids [µg/mL]: <0.05
- REF HYB-5252 DRG:HYBRiD-XL Analyzer
- REF HYI-5392: *System Solution 5L*, 5000 mL;
  (Instrument Feed Water according to CLSI guideline 3C-A4 with the following specification can also be used:
  Resistivity at 25 °C [MΩ·cm]: > 1
  Conductivity at 25 °C [µS·cm^{-1}]: < 1
  Total Organic Carbon/p.p.b.[µg/L] : < 200
  Colloids [µg/mL]: <0.1)
- REF HYI-5394: *Wash Buffer*, 40x concentrate, 25 mL
- REF HYI-5395: *Needle Cleaning Solution*, 30 mL. Cleaning solution for the pipetting needle (daily and weekly maintenance, see also user manual)
- REF HYI-5387: *Cuvettes*, (2 x 360 pieces)

For use of the *Secondary Sample Holder* for secondary tubes the following tubes are required:

- REF HYI-5391: *Sample Tubes (Secondary)*, 2500 pcs.

4.3 Storage Conditions

All kit components should be stored at 2 °C to 8 °C to ensure product performance until the defined expiry date.

When stored at 2 °C to 8 °C, **unopened kits** will retain reactivity until expiration date. Do not use reagents beyond this date.

- Cartridges (stored at 2 °C to 8 °C) in the supplied and unopened zip/foil bags will retain reactivity until expiration date.
- Unopened Re-Calibrators and Controls (stored at 2 °C to 8 °C) will retain reactivity until expiration date.

Opened reagents and the reagent cartridges must be stored at 2 °C to 8 °C.
Once the plastic bag has been opened, care should be taken to tightly close it again along with the supplied desiccant bag.
Immediately after end of each run the Re-Calibrator and Control vials have to be removed from the instrument, tightly capped and stored at 2 °C to 8 °C.

- Unused cartridges in opened zip/foil bags (stored at 2 °C to 8 °C) will retain reactivity until expiration date, if stored as described above.
- Pierced or open cartridges must be disposed of immediately.
- Opened Re-Calibrators and Controls (stored at 2 °C to 8 °C) will retain reactivity for 8 weeks.

4.3.1 On-board Stability

For Re-Calibrators and Controls the on-board stability has been evaluated under controlled laboratory conditions at room temperature (20 °C to 25 °C).
Due to the differences in laboratory environmental conditions and reagent volumes, the on-board stability may deviate from the declared value.

On-board stability:	8 h

4.4 Reagent Preparation

Bring all reagents, such as controls and re-calibrators, to room temperature (20 °C to 25 °C) prior to use. Reagent Cartridges can be used directly after storage in the refrigerator.

***Wash Buffer* (not included in the kit)**

For Wash Buffer (1x) dilute 25 mL of *Wash Buffer* (40x) with 975 mL ultra-pure water to a final volume of 1000 mL.
The diluted Wash Buffer (1x) is stable for 2 weeks at room temperature.

4.5 Disposal of the Kit

The disposal of the kit and all used materials/reagents must be performed according to the national regulations. Special information for this product is given in the Safety Data Sheet.

4.6 Damaged Test Kits

In case of any damage to the test kit or components, DRG must be informed in writing, at the latest one week after receiving the kit. Damaged single components should not be used for a test run. They have to be stored until a final solution has been found. After this, they should be disposed of according to the official regulations.

5 SPECIMEN COLLECTION AND PREPARATION

Saliva can be used in this assay.

Eating, drinking, chewing gums or brushing teeth should be avoided for 30 minutes before sampling. Otherwise, it is recommended to rinse mouth thoroughly with cold water 5 minutes prior to sampling.
Do not collect samples when oral diseases, inflammation or lesions exist (blood contamination).
If there is visible blood contamination in the patient specimen, it should be discarded. Rinse the sampling device with water, wait for 10 minutes and take a new sample.
Note: Samples containing sodium azide should not be used in the assay.

A minimum of 160 µL of saliva supernatant (see chapter 5.2) is needed for one determination. This includes 100 µL sample and 60 µL dead volume.

5.1 Specimen Collection

Cortisol production follows a circadian rhythm. Levels peak in the early morning and drop to the lowest concentration at night.
Collection time must be noted in order to choose appropriate reference ranges.
Saliva samples should be collected using SALI-TUBES 100 (REF SLV-4158).
Other saliva sampling devices have not been tested and should be validated under the responsibility of the user.

5.2 Specimen Storage and Preparation

Fresh saliva samples
Immediately after arrival in the lab, fresh saliva samples should be **frozen at least overnight at -20 °C**.
Each saliva sample has to be frozen, thawed, and centrifuged in order to separate the mucins by centrifugation.
Storage: immediately at -20 °C for up to 3 months.

Then samples must be thawed and centrifuged for 5 to 10 minutes at 10 000 *g*.
Thereafter, the clear supernatant must be transferred into a fresh tube.
Only this clear supernatant can be used as sample for the ELISA.

Supernatant
Storage: 7 days at 2 °C to 8 °C
up to 12 months at -20 °C

The supernatant should be frozen only once.
Thawed supernatant should be inverted several times prior to testing!

5.3 Specimen Dilution

5.3.1 Manual Sample Dilution

If in an initial assay, a specimen is found to contain more than the highest standard, the specimens can be diluted with *Sample Diluent** and measured again as described in Assay Procedure.
For the calculation of the concentrations this dilution factor has to be taken into account.
Example:
a) dilution 1:10: 10 µL sample + 90 µL *Sample Diluent* (mix thoroughly)
b) dilution 1:100: 10 µL dilution a) 1:10 + 90 µL *Sample Diluent* (mix thoroughly).

* *Sample Diluent for manual dilution is not included in this kit, but can be ordered on request (REF HYE-5344-DIL, 20 mL).*

6 ASSAY PROCEDURE

6.1 General Remarks

- All reagents, such as controls and re-calibrators and specimens, must be allowed to come to room temperature (20 °C to 25 °C) before use.
  All reagents and samples must be mixed without foaming.
  Reagent Cartridges can be used directly after storage in the refrigerator.
- Samples, controls and re-calibrators should be measured within 2 hours in order to avoid possible evaporation effects.
- The Secondary Sample Holder (HYI-5437) for secondary tubes has the capacity for a maximum of 20 samples including controls and re-calibrators. They all have to be pipetted into the secondary tubes, and the respective barcodes of control/re-calibrator vials and, if available, the sample barcodes have to be read with the external barcode scanner.

6.2 Test Procedure

- **The total assay time for DRG:HYBRiD-XL Salivary Cortisol is 150 minutes.**
- To ensure proper operation of the test, the instructions in the user manual for the DRG:HYBRiD-XL should strictly be followed.
- All test specific information required for the correct operation is included in the respective barcodes of the reagents.
  Take care not to damage these bar codes!
- **It is recommended to tap the bottom of the Cartridge Segments containing the reagent cartridges once on the bench before placing them on the rotor. This is to avoid foam and adhering of the liquid on the sealing of the reagent cartridge.**
- Place reagent cartridges on the rotor of the unit. The heating to 37 °C incubation temperature is performed automatically in the unit.

6.3 Calibration

Traceability:

This method was standardized against the following reference material:
C-106 (Cerilliant)

Each DRG:HYBRiD-XL reagent contains a barcode with the specific information for recalibration of the reagent lot. The Master Curve is printed as a 2-D barcode on the outer label of the kit package and on the QC-Datasheet and has to be scanned with the external barcode scanner prior to the first use of the respective kit lot.

Recalibration is recommended:

- if a new kit lot is used. Each new lot should be verified by running the kit internal re-calibrators and controls before routine use.
- if one or both assay controls are found outside the specified range.
- after 4 weeks of use of the same reagent kit on the unit.

6.4 Calculation of Results

The analyte concentrations are calculated automatically by the DRG:HYBRiD-XL's system software.

7 QUALITY CONTROL

It is recommended to use control samples according to state and federal regulations. The use of control samples is advised to assure the day to day validity of results.

It is also recommended to participate in national or international Quality Assessment programs in order to ensure the accuracy of the results.

Apply appropriate statistical methods for analysing control values and trends. If the results of the assay do not agree with the established acceptable ranges of control materials, patient results should be considered invalid. In this case, please check the following: expiration dates and storage conditions of reagents, operational reliability of the analyser. In addition, it is indicated to perform a Recalibration.

In case of further questions please contact your local distributor or DRG directly.

7.1 Internal Controls

For Quality Control it is necessary to use the two internal controls provided with each kit.

Acceptance ranges for both internal controls (*Control 1 & 2*) were established by the manufacturer and are summarized in the QC-Datasheet added to the kit. Note that the expected values and acceptance ranges stated in the QC-Datasheet always refer to the current kit lot.

Internal controls should be run in single determination:

- on a routine basis (e.g. once per 24 h)
- if re-calibration is required (if one or both internal controls are out of range)
- if a new kit lot is used (in order to avoid any negative impact on the kit performance by improper transport or to detect improper storage during transport).

7.2 External Controls

Use controls at both normal and pathological levels.

The control intervals and control ranges for external controls should be adapted to the individual requirements of each laboratory. All results must be within the defined limits.

Each laboratory should establish corrective measures to be taken if values of external controls are not found in the acceptance range.

8 EXPECTED NORMAL VALUES

It is strongly recommended that each laboratory should determine its own normal and pathological values.

In a study conducted with apparently healthy individuals, using the DRG:HYBRiD-XL Salivary Cortisol the following data were observed:

Population	Total
n	120
Range (min. - max.) (ng/mL)	0.28 – 9.74
Mean (ng/mL)	5.02
2.5^{th} - 97.5^{th} Percentile (ng/mL)	1.44 – 9.10
Median (ng/mL)	4.81

120 samples (60 males and 60 female) were collected between 7 a.m. and 7 p.m. Percentiles, mean and median reflect the overall range of values.

The results alone should not be the only reason for any therapeutic consequences. The results should be correlated with other clinical observations and diagnostic tests.

9 LIMITATIONS OF USE

Reliable and reproducible results will be obtained, when the assay procedure is performed with a complete understanding of the instructions for use and with adherence to good laboratory practice.

Any improper handling of samples or modification of this test might influence the results.

10 PERFORMANCE CHARACTERISTICS

10.1 Assay Dynamic Range

The dynamic range of the assay is defined by the limit of detection and the maximum value of the Master Curve.

Values found below the measuring range are indicated as "< 0.10 ng/mL".

Values found above the measuring range are indicated as "> 30 ng/mL".

The measuring range of the assay is between 0.10 ng/mL – 30 ng/mL.

10.2 Specificity of Antibodies (Cross-Reactivity)

The following substances were tested for cross-reactivity of the assay:

Substance	Added Conc. (ng/mL)	Measured Conc. (ng/mL)	Cross-reactivity (%)
Androstenedione	10.00	0.7	0.70
Corticosterone	1.00	0.38	38.00
Estrone	0.33	0.0	< 0.001
Estradiol	0.10	0.0	< 0.001
Estriol	40.00	0.0	< 0.001
DHEA	1.44	0.0	< 0.001
DHEA-S	10000.00	1.33	0.01
Progesterone	2.40	0.02	0.69
Testosterone	1.00	0.00	< 0.001

10.3 Sensitivity

The sensitivity study was designed according to CLSI guideline EP17-A2.

The Limit of Blank (LoB) is 0.02 ng/mL.

The Limit of Detection (LoD) is 0.10 ng/mL.

The Limit of Quantification (LoQ) is 0.28 ng/mL.

10.4 Precision Performance

The precision study was designed on the basis of to CLSI guideline EP5-A2.

10.4.1 Intra-Device Precision

The Intra-Device precision was determined with 4 patient samples covering the complete measuring range in 5 independent runs within 5 days with 2 different devices in 5 replicates per run. CV was calculated as mean CV of 10 runs.

The intra-device variability is shown below:

Sample	n	Mean (ng/mL)	CV (%)
1	10	0.80	6.25
2	10	3.65	3.42
3	10	9.44	2.78
4	10	20.25	1.29

10.4.2 Inter-Device Precision

The Inter-Device precision was determined for 4 patient samples covering the measuring range in 5 independent runs on 5 days with 2 different devices in 5 determinations per run. CV was calculated from 50 determinations.

The inter-device variability is shown below:

Sample	n	Mean (ng/mL)	CV (%)
1	50	0.80	13.74
2	50	3.65	12.00
3	50	9.44	6.43
4	50	20.25	3.09

10.4.3 Inter-Lot

The between-lots variation was determined by 6 measurements of 4 samples with 3 different kit lots.

Sample	n	Mean (ng/mL)	CV (%)
1	18	1.56	5.84
2	18	9.60	6.07
3	18	19.39	6.23
4	18	16.56	3.94

10.5 Recovery

Recovery was determined by adding four increasing concentrations of the analyte to four different patient samples containing different amounts of endogenous analyte. Each sample (non-spiked and spiked) was assayed and analyte concentrations of the samples were calculated from the Master Curve. The percentage recoveries were determined by comparing expected and measured values of the samples.

Sample		1	2	3	4
Concentration (ng/mL)		1.92	6.53	8.41	14.45
Average Recovery (%)		98.0	97.2	103.2	104.3
Range of Recovery (%)	from	88.4	94.4	100.8	97.4
	to	104.7	101.7	104.8	111.8

10.6 Linearity

Four samples containing different amounts of analyte were serially diluted with *Sample Diluent*. The percentage recovery was calculated by comparing the expected and measured values for the analyte.

Sample		1	2	3	4
Concentration (ng/mL)		2.37	8.50	16.15	22.00
Average Recovery (%)		102.8	90.1	98.9	101.4
Range of Recovery (%)	from	90.3	89.0	97.6	95.1
	to	110.0	91.4	100.6	109.5

10.7 Interfering Substances

Until today no substances (drugs) are known to us, which have an influence to the measurement of cortisol in a sample.

10.8 High-Dose-Hook Effect

No hook effect was observed in this test.

11 METHOD COMPARISON

A comparison of DRG:HYBRiD-XL Salivary Cortisol Test (HYE-5344) (y) and the FDA approved DRG Salivary Cortisol ELISA (SLV-2930) (x) using clinical samples gave the following correlation:

n = 43
r = 0.990
y = 0.925x + 0.357

A comparison of DRG:HYBRiD-XL Salivary Cortisol Test (HYE-5344) (y) and LC-MS/MS (x) using clinical samples gave the following correlation:

n = 11
r = 0.999
y = 1.139x - 0.139

12 LEGAL ASPECTS

Only for countries where the declaration of European Conformity (CE mark) is applicable.

12.1 Reliability of Results

The test must be performed exactly as per the manufacturer's instructions for use. Moreover, the user must strictly adhere to the rules of GLP (Good Laboratory Practice) or other applicable national standards and/or laws. This is especially relevant for the use of control reagents. It is important to always include, within the test procedure, a sufficient number of controls for validating the accuracy and precision of the test.

The test results are valid only if all controls are within the specified ranges and if all other test parameters are also within the given assay specifications. In case of any doubt or concern please contact DRG.

12.2 Therapeutic Consequences

Therapeutic consequences should never be based on laboratory results alone even if all test results are in agreement with the items as stated under point 12.1. Any laboratory result is only a part of the total clinical picture of a patient.

Only in cases where the laboratory results are in acceptable agreement with the overall clinical picture of the patient should therapeutic consequences be derived.

The test result itself should never be the sole determinant for deriving any therapeutic consequences.

12.3 Liability

Any modification of the test kit and/or exchange or mixture of any components of different kit lots could negatively affect the intended results and validity of the overall test. Such modification and/or exchanges invalidate any claim for replacement.

Claims submitted due to customer misinterpretation of laboratory results subject to point 12.2 are also invalid. Regardless, in the event of any claim, the manufacturer's liability is not to exceed the value of the test kit. Any damage caused to the test kit during transportation is not subject to the liability of the manufacturer.

For further information please refer to the User Manual of the DRG:HYBRiD-XL, analyser-specific application sheets, product information and package inserts of all necessary components.

13 REFERENCES / LITERATURE / LITERATUR / BIBLIOGRAFIA / LITERATURA / BIBLIOGRAFIA

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SYMBOLS USED

Symbol	English	Deutsch	Italiano	Español	Français	Polski
CE	European Conformity	CE-Konformitäts-kennzeichnung	Conformità europea	Conformidad europea	Conforme aux normes européennes	Zgodność z normami europejskimi
	Consult instructions for use*	Gebrauchsanweisung beachten*	Consultare le istruzioni per l'uso	Consulte las Instrucciones	Consulter les instructions d'utilisation	Zapoznać się z instrukcją użytkowania
IVD	*In vitro* diagnostic medical device*	*In-vitro*-Diagnostikum*	Per uso Diagnostica in vitro	Para uso Diagnóstico in vitro	Usage Diagnostic in vitro	Wyrób medyczny do diagnostyki in vitro
RUO	For research use only	Nur für Forschungszwecke	Solo a scopo di ricerca	Sólo para uso en investigación	Seulement dans le cadre de recherches	Tylko do użytku w badaniach
REF	Catalogue number*	Artikelnummer*	No. di Cat.	Número de catálogo	Référence	Numer katalogowy
LOT	Batch code*	Chargencode*	Lotto no	Número de lote	No. de lot	Numer LOT
	Contains sufficient for <n> tests *	Ausreichend für <n> Prüfungen *	Contenuto sufficiente per "n" saggi	Contenido suficiente para <n> ensayos	Contenu suffisant pour "n" tests	Zawartość przeznaczona na <n> testów
	Temperature limit*	Temperatur-begrenzung*	Temperatura di conservazione	Temperatura de conservacion	Température de conservation	Przechowywać w temperaturze
	Use-by date*	Verwendbar bis*	Data di scadenza	Fecha de caducidad	Date limite d'utilisation	Data przydatności
	Manufacturer*	Hersteller*	Fabbricante	Fabricante	Fabricant	Producent
	Caution*	Achtung*				UWAGA
Distributed by	Distributor	Vertreiber	Distributore	Distribuidor	Distributeur	Dystrybutor
Content	Content	Inhalt	Contenuto	Contenido	Contenu	Zawartość
Volume/No.	Volume / No.	Volumen/Anzahl	Volume/Quantità	Volumen/Número	Volume/Numéro	Objętość / Numer
Reagent Cartridge	Reagent Cartridge	Reagenzien-Cartridge	Cartucce di reagente	Cartucho de reactivo	Cartouche de réactif	Kartridż z odczynnikami
Re-Calibrator	Re-Calibrator	Re-Kalibrator	Re-Calibratore	Re-Calibrador	Re-calibrateurs	Re-kalibrator
Control	Control	Kontrolle	Controllo	Control	Contrôle	Kontrola
Enzyme Conjugate	Enzyme Conjugate	Enzymkonjugat	Coniugato enzimatico	Conjugado enzimático	Conjugué enzymatique	Koniugat enzymatyczny
Enzyme Complex	Enzyme Complex	Enzymkomplex	Complesso enzimatico	Complex enzimático	Complexe enzymatique	Kompleks Enzymu
Substrate Solution	Substrate Solution	Substratlösung	Soluzione di substrato	Solución de sustrato	Solution substrat	Roztwór Substratu
Sample Diluent	Sample Diluent	Probenverdünnungs-medium	Diluente dei campioni	Solución para dilución de la muestra	Diluant d'échantillon	Rozcieńczalnik Próbki
Reagent 1	Reagent 1	Reagenz 1	Reagente 1	Reactivo 1	Réactif 1	Reagent 1
Reagent 2	Reagent 2	Reagenz 2	Reagente 2	Reactivo 2	Réactif 2	Reagent 2
Wash Buffer	Wash Buffer	Waschpuffer	Tampone di lavaggio	Tampón de lavado	Tampon de lavage	Bufor Płuczący
System Solution	System Solution	Systemlösung		Solución de sistema	Solution système	Roztwór systemowy
Needle Cleaning Solution	Needle Cleaning Solution	Nadel-Reinigungslösung	Soluzione lavaggio ago	Solución de lavado de la aguja	Solution de nettoyage des aiguilles	Roztwór Czyszczący Igły
Denaturation Buffer	Denaturation Buffer	Denaturierungspuffer	Tampone die denaturazione	Tampón de denaturalización	Tampon de dénaturation	Bufor do Denaturacji
Neutralization Buffer	Neutralization Buffer	Neutralisierungspuffer	Tampone di neutralizzazione	Tampón de neutralización	Tampon de neutralisation	Bufor Neutralizujący
Assay Buffer	Assay Buffer	Assaypuffer	Tampone del test	Tampón de ensayo	Tampon d'essai	Bufor testowy
Conjugate Buffer	Conjugate Buffer	Konjugatpuffer	Tampone del coniugato	Tampón de conjugado	Tampon de conjugué	Roztwór koniugatu
Secondary Sample Holder	Secondary Sample Holder	Sekundärprobenhalter	Sostegno secondario dei campioni	Soporte de muestras para tubos secundarios	Support d'échantillons secondaires	Statyw na probówki drugorzędowe
Sample Tubes (Secondary)	Sample Tubes (Secondary)	Sekundärproben-röhrchen	Tubetti di campioni secondari	Tubos de muestra secundarios	Tubes échantillon secondaires	Probówki drugorzędowe
Dilution Cartridge	Dilution Cartridge				Cartouches de dilution	Kartridż do rozcieńczeń
Vial Adapter	Vial Adapter	Fläschchen-Adapter	l'adattatore dei tubetti	Adaptador de tubos	l'Adaptateur de flacons	Nakładki na butelki dla kontroli i kalibratorów