

RIDA[®]QUICK Verotoxin/O157 Combi

New and unique diagnostic options in the identification of STEC/EHEC in stool specimens



Verotoxin- and Shiga toxin-producing *E. coli* strains cause a broad spectrum of illnesses that may vary in intensity and manifestation. This spectrum reaches from mild, watery diarrhoea at one end of the range, via bloody, violent diarrhoea, all the way to hemolytic-uremic syndrome (HUS) with acute kidney damage at the other. Depending on the constellation of the virulence factors of STEC, in this extreme case the diagnosis is EHEC, which produce not only shigatoxin genes but also intimin and enterohemolysin.

The severe hemorrhagic courses predominantly affect children up to five years of age 3 – 5 % die of renal failure. A major part of the surviving children may go on to suffer from the sequelae of an EHEC infection for the rest of their life, with hypertension and impaired renal function.

The pathogens are transmitted by the consumption of products from farm animals (goats, sheep, pigs) and wild animals, but mainly by contaminated beef products (meat and milk). Direct contact with infected people and animals as well as swimming in water contaminated with faecal matter also constitute potential routes of infection.

Besides the use of molecular methods for the detection of the Shiga toxin genes and of other virulence markers, the identification of the two Shiga toxins (Stx1/Stx2) and their variants using ELISA methods has established in the diagnosis of persons infected with STEC/EHEC. Regarding the ELISA methods it is important that all human-pathological variants of the two Shiga toxins are captured.

Furthermore, the specific detection of the former EHEC prototype and the most commonly occurring variant, serovar O157, by means of selective culture media is well established.

Besides a multitude of other Shiga toxin-forming serovars, O157 is the most frequently detected agent, both in sporadic infections as well as in epidemic situations. In HUS patients, this serotype is identified as being the causative agent of the illness in the majority of all cases. Today, the demand for an immediate separation of paediatric

STEC O157 patients from their relatives or other patients is seen as possessing a high preventive potential in the efforts to prevent any further spread. However, this requires a method for the immediate and simultaneous identification of both Shiga toxins as well as O157 that extends beyond the current laboratory standard.

The classic *E. coli* strain O157:H7 serotype, which was for many years the one used in the United States and in many other countries as a synonym for EHEC (STEC O157), has undergone transformation. New rapid diagnosis methods must be made available.

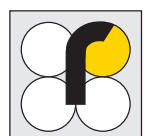
Cultivation on sorbitol-MacConkey agar (SMAC) is not sufficient any longer. Whereas the classic variant O157:H7 - due to its inability to utilize sorbitol - can be easily distinguished from the other enterobacteria, there are today new variants of this serovar, which can not be distinguished on SMAC. Those variants are characterized by the capability of metabolization of sorbitol, but also by an altered constellation of virulence factors and the absence of flagella.

In about 5 % of all HUS patients, EHEC strains were detected that deleted the Stx gene in the host during the infection. Roughly 40 % of such isolates belonged to the O157 serotype and were without exception immobile (Bielaszewska et al., 2007). Most of the O157 isolates were capable to metabolize sorbitol, while slightly more than 10 % - similar to the classic O157:H7 variant - were still sorbitol-negative.

The deletion of the Stx gene during infection shows just how swiftly genetic transformation can take place. EHEC that caused a severe illness can transform into a less hazardous pathogen, one that due to the lack of Shiga toxin formation is suddenly capable of causing only milder forms of diarrhoea (Friedrich et al., 2007).

Detection of the most relevant serovar, O157, in parallel to the identification of Shiga toxin is closing the diagnostic gap now.

The new RIDA[®]QUICK Verotoxin/O157 Combi rapid test takes this into account. Within 20 minutes it enables the specific identification of the O157 antigen, while at the same time capturing all human-pathological Shiga toxin variants from one stool-enrichment culture with mitomycin C-containing mTSB broth.



It is possible to track down, within one day the cause of a diarrhoea illness mediated by Shiga toxin and/or O157 variants, and to initiate the appropriate therapeutic measures.

Preliminary studies have provided impressive proof of the advantages of this dual EHEC/STEC-diagnostic method (Mellmann et al., Poster ECCMID 2008).

The poster is available as a pdf download upon request.

RIDA®QUICK Verotoxin/O157 Combi
Art. No. N2202 (strips)
Art. No. N2203 (cassettes)

¹ *Bielaszewska M. et al. (2007) Shiga Toxin-mediated Hemolytic Uremic Syndrome: Time to change the diagnostic paradigm? Plos one, 10 : e1024.*

² *Friedrich A. et al. (2007) Prevalence, virulence profiles and clinical significance of Shiga toxin-negative variants of enterohemorrhagic Escherichia coli O157 infections in humans. Clin Infect Dis 45: 39 – 45.*

³ *Mellmann A. et al. (2008) Evaluation of the RIDA®QUICK Verotoxin / O157 Combi for the detection Shiga Toxin and Escherichia coli O157 in stool enrichment cultures. Poster, presented at 18th ECCMID in Barcelona.*

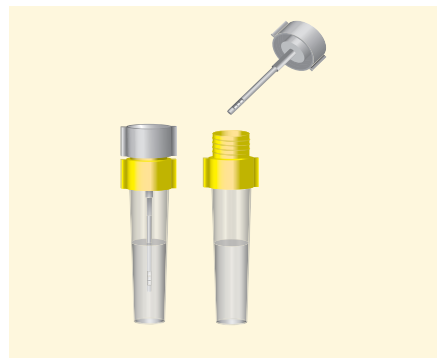
New RIDASCREEN® stool sampling tube enables specimens to be taken simply and eases the stool-processing steps

R-Biopharm has developed and validated a stool-processing tube that optimizes and accelerates the testing procedures. It is specially designed for use with the RIDASCREEN® Haemoglobin and RIDASCREEN® Haemo-/Haptoglobin Complex tests.

The RIDASCREEN® stool sampling tube, filled with RIDASCREEN® Stool Extraction Buffer, is now available for ordering.

Advantages of the RIDASCREEN® stool sampling tube:

- Simple and clean taking of stool specimens
- Clean and safe dilution of the stool sample
- Coefficient of variation approx. 4% – better than other extraction methods.
- To dissolve the stool specimen, the tube must just be shaken and the contents immediately pipetted into the microtitre well – no centrifuging necessary
- No predilution necessary – the sample is diluted directly in the microtitre well



Further R-Biopharm tests are currently undergoing validation with the RIDASCREEN® stool sampling tube.

RIDASCREEN® stool tubes
Art. No. GZ 3002

Continous success of RIDA® AllergyScreen worldwide

The RIDA® AllergyScreen is a panel test for performing 20 different allergens in one shot.

Panel testing enables an accurate and more comprehensive diagnosis in a wide range of varying symptoms and sensitization patterns against several allergens. A definitive diagnosis of confirmed allergic disease offers several benefits for patients such as unnecessary trials of allergy medication.

The 4 standard panels cover the most common allergens in the central European countries. In order to be successful worldwide R-Biopharm offers country-specific panels meeting the special needs of the local allergenic situation. This is one of the principal reasons for the huge success of RIDA® AllergyScreen worldwide. Another main product feature is that the immobilized allergens are not covalently bound to the membrane and kept therefore more in its native structure.

Two new countries have launched the RIDA® AllergyScreen in their market recently:

India and Iran. Due to a changing lifestyle combined with a higher consumption of industrialized food the prevalence of allergies is increasing worldwide, including India and Iran. In India panel testing is highly appreciated because of its high efficiency. The results are reliable and comparable with other systems even with the Skin Prick Test.

In Iran the needs are similar. Iran has a network of allergologists and numerous allergy hospitals. RIDA® AllergyScreen was introduced at first in a children's hospital, because the low volume of serum needed is regarded as a crucial advantage in the paediatric allergy diagnostics. Panel tests are convenient for determination of allergies in children. Namely children show often a wide range of varying symptoms and sensitization pattern against several allergens. Together with the local organisation and the clinicians an allergy project is just initiated in order to figure out the most important allergens in Iran. After finishing this project an Iranian panel will be created with these allergens.

We welcome India and Iran in the world of RIDA® AllergyScreen.

Cooperation with Mikrogen GmbH in the infection serology area

With effect from April this year, our ELISA serology products in Germany will be exclusively marketed by the company Mikrogen GmbH in Neuried near Munich. We are delighted that we have found in Mikrogen a sales partner who for many years now has been contributing to improvements in infection-serology diagnosis with its innovative developments in the area of recombinant antigens. Western blots and line blots supplied by Mikrogen are known for their excellent quality and are used as confirmatory tests in many laboratories. As screening tests with comparable quality claims, our ELISA products constitute an ideal supplement. Both companies are convinced that the cooperation will enable us to

offer our customers high-quality system solutions from just one supplier in the future.

The sales cooperation shall not entail any changes or inconveniences for our present customers. If you have ordered ELISA products or other tests (IFT, western blots) from R-Biopharm in the past, we shall naturally continue to supply you with the corresponding products, and your familiar contacts with our sales team and the order-processing department shall remain responsible for tending to your needs. There shall hence be no changes regarding your purchase activities or your documentation operations in the laboratory.

Diagnostics company R-Biopharm AG builds company HQ in Pfungstadt, Germany

1. April 2008

R-Biopharm AG is proud to lay the foundations for its new headquarters in Pfungstadt, located south of Darmstadt. The diagnostics company, whose current premises in the Landwehrstraße, Darmstadt, have become too small, has invested 22 million Euros in the industrial estate.

R-Biopharm AG was founded in 1988 as a subsidiary of Röhm GmbH and was taken over in a management buy out in 1991 by Dr. Ralf M. Dreher. With its innovative detection systems, the company is a leading provider of analytical test kits. R-Biopharm distributes its products globally and currently has nine international subsidiaries. The key competencies lie in the in-house development, production and sales of highly sensitive and specific products.

At present, the offices, laboratories, production, quality assurance and storage are in a 6,000 sqm large area in the Landwehrstraße in Darmstadt, where 180 people are currently employed. For lack of space, one part of the labs had to be temporarily

housed in the previous premises in Dolivostrasse, in 2007. The future company building will cover an area of 14,000 sqm and is designed for around 350 employees, thus uniting all divisions under one roof.

Building size

Element	Approx. size in sqm
Office and canteen	3,891
Labs and offices	3,768
Production (with lab and offices)	3,991
Warehouse (partly high-rise storage)	1,637
Engineering	729
Sum	14,016
Parking spaces	150

Specialist consultants

Architects: Jean Vassiliadis, Deutsche Baumanagement GmbH, Düsseldorf

General planners: Deutsche Baumanagement GmbH, Düsseldorf

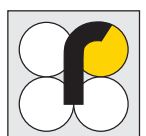
Main contractor: Baresel GmbH, Leinfelden Echterdingen



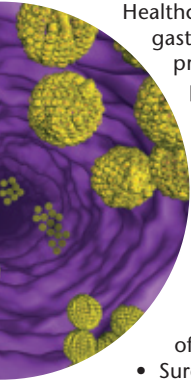
South view of the new company headquarters in Pfungstadt

If you are interested in our products,
please contact your local distributor.

r-biopharm



Norovirus Outbreaks cause high Costs in hospitals and nursing homes



Healthcare-associated outbreaks of gastroenteritis are an increasing problem. The following measures put even more pressure on limited budgets of healthcare facilities:

- Shut-down of complete hospital departments
- Transient stop of the admission of new patients
- Sick-leave of nursing staff and physicians lead to the detraction of service schedules
- Surgeries have to be delayed or dropped
- Extended bed times and delayed release of patients, therefore often over-allocation of beds
- Increased efforts for hygiene arrangements

A very good study of the National Health Service of England (GB) published by Lopman et al. (Emerging Infections Diseases, Vol 10, No. 10, Oct 2004; www.cdc.gov/eid) has estimated the costs caused by nosocomial gastroenteritis.

The largest group of outbreaks was caused by Norovirus (63%), in a few cases in double infection together with *Clostridium difficile*. Other determined pathogens were Rotavirus and *Campylobacter*.

The Shut-down of complete hospital departments (on average for 10 days), unavailability of beds and the absence of nursing staff and physicians due to sick leave generate annual costs of about 184 Mio US\$ (or 1.01 Mio. US\$ per 1000 hospital beds).

About 12 % of over-all costs caused by nosocomial infections in hospitals and nursing homes are derived by gastroenteritis cases. The study clearly indicates that a very quick and reliable diagnosis of gastroenteritis is beneficial, but this methods should be applicable for routine laboratories.

In a suspected outbreak, samples have to be analyzed close to the initial infection and results should be available after short time to decide to start suitable hygiene measures immediately. In addition a quick determination whether the outbreak is induced by bacterial or viral pathogens is needed to start a targeted medicinal therapy.

Fairs and conferences



29.07. – 31.07.2008

AACC 2008 Clinical Lab Expo
in Washington, DC, USA, Washington Convention Center

11.12. – 12.12.2008

The LANCET Conference Healthcare-associated infections
QE11 Conference Centre, London, UK

R-Biopharm^{news} is edited by

R-Biopharm AG
Landwehrstrasse 54, 64293 Darmstadt
Germany
Phone: +49 61 51 - 81 02-0
Fax: +49 61 51 - 81 02-40
www.r-biopharm.com

r-biopharm

