

## Appendix 1: EHEC and HUS

### Overview

*Escherichia coli* (*E. coli*) is a bacterium that is commonly found in the gut of humans and warm-blooded animals. Most strains of *E. coli* are harmless. Some strains however, such as enterohaemorrhagic *E. coli* (EHEC), can cause severe foodborne disease. It is transmitted to humans primarily through consumption of contaminated foods, such as raw or undercooked ground meat products, raw milk and contaminated raw vegetables and shoots. Its significance as a public health problem was recognized in 1982, following an outbreak in the United States of America.

EHEC produces toxins known as verotoxins or Shiga-like toxins because of their similarity to the toxins produced by *Shigella dysenteriae*. EHEC can grow in temperatures ranging from 7°C to 50°C, with an optimum temperature of 37°C. Some EHEC can grow in acidic foods, down to a pH of 4.4, and in foods with a minimum water activity ( $A_w$ ) of 0.95. It is destroyed by thorough cooking of foods until all parts reach a temperature of 70°C or higher. *E. coli* O157:H7 is the most important EHEC serotype in relation to public health; however, other serotypes have frequently been involved in sporadic cases and outbreaks.

### Symptoms

Symptoms of the diseases caused by EHEC include abdominal cramps and diarrhoea that may in some cases progress to bloody diarrhoea (haemorrhagic colitis). Fever and vomiting may also occur. The incubation period can range from three to eight days, with a median of three to four days. Most patients recover within 10 days, but in a small proportion of patients (particularly young children and the elderly), the infection may lead to a life-threatening disease, such as haemolytic uraemic syndrome (HUS). HUS is characterized by acute renal failure, haemolytic anaemia and thrombocytopenia. It is estimated that up to 10% of patients with EHEC infection may develop HUS, with a case-fatality rate ranging from 3 to 5%. Overall, HUS is the most common cause of acute renal failure in young children. It can cause neurological complications (such as seizure, stroke and coma) in 25% of HUS patients and chronic renal sequelae, usually mild, in around 50% of survivors.

Persons who experience bloody diarrhoea or severe abdominal cramps should seek medical care. Antibiotics are not part of the treatment of patients with EHEC disease and may possibly increase the risk of subsequent HUS.

### Sources and transmission

Most available information on EHEC relates to serotype O157:H7, since it is easily differentiated biochemically from other *E. coli* strains. The reservoir of this pathogen appears to be mainly cattle. In addition, other ruminants such as sheep, goats and deer are considered significant reservoirs, while other mammals (pigs, horses, rabbits, dogs and cats) and birds (chickens, turkeys) have occasionally been found infected.

*E. coli* O157:H7 is transmitted to humans primarily through consumption of contaminated foods, such as raw or undercooked ground meat products and raw milk. Faecal contamination of water and other foods, as well as cross-contamination during food preparation (with beef and other meat products, contaminated surfaces and kitchen utensils), will also lead to infection. Examples of foods implicated in outbreaks of *E. coli* O157:H7 include undercooked hamburgers, dried cured salami, unpasteurized fresh-pressed apple cider, yogurt, and cheese made from raw milk.

An increasing number of outbreaks are associated with the consumption of fruits and vegetables (shoots, spinach, lettuce, coleslaw and salad) whereby contamination may be due to contact with faeces from domestic or wild animals at some stage during cultivation or handling. EHEC has also been isolated from bodies of water (ponds, streams), wells and

water troughs, and has been found to survive for months in manure and water-trough sediments. Waterborne transmission has been reported, both from contaminated drinking-water and from recreational waters.

Person-to-person contact is an important mode of transmission through the oral-faecal route. An asymptomatic carrier state has been reported, where individuals show no clinical signs of disease but are capable of infecting others. The duration of excretion of EHEC is about one week or less in adults, but can be longer in children. Visiting farms and other venues where the general public might come into direct contact with farm animals has also been identified as an important risk factor for EHEC infection.

#### Prevention

The prevention of infection requires control measures at all stages of the food chain, from agricultural production on the farm to the processing, manufacturing and preparation of foods in both commercial establishments and household kitchens.

#### Household

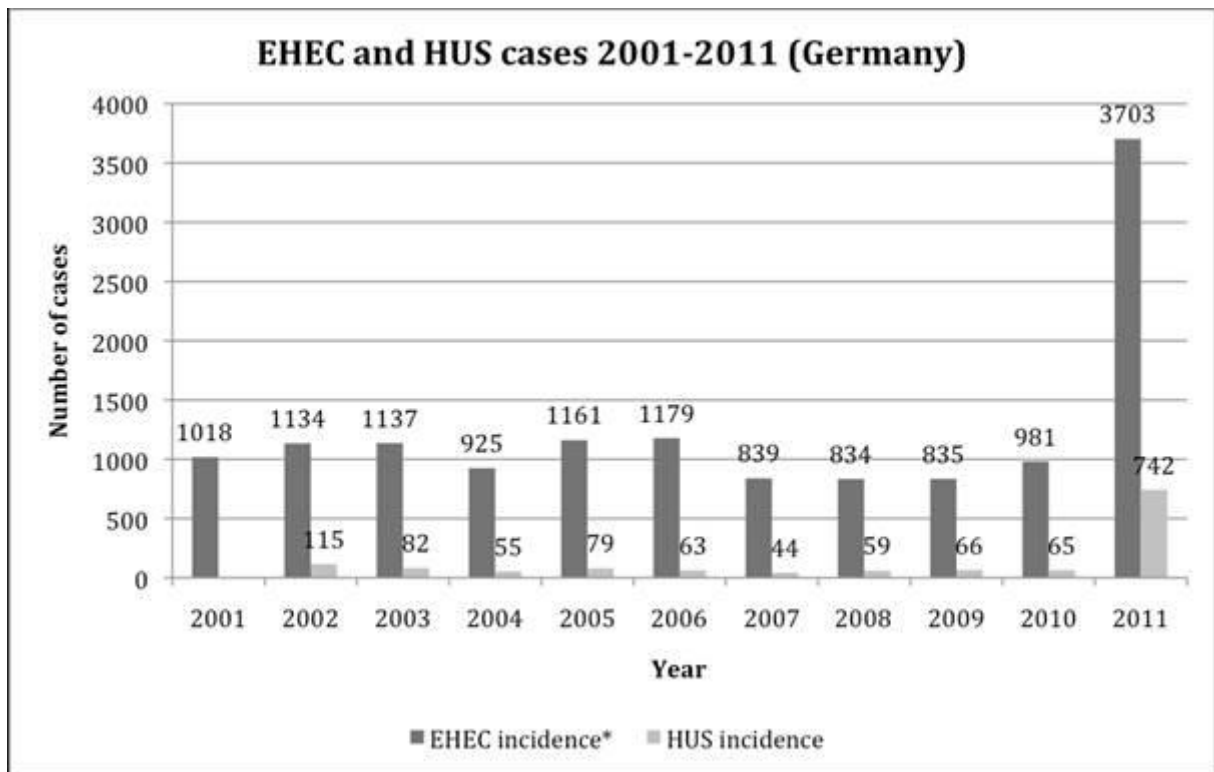
Preventive measures against *E. coli* O157:H7 infections are similar to those recommended for other foodborne diseases. Basic good food hygiene practice, as described in the WHO Five keys to safer food, can prevent the transmission of pathogens responsible for many foodborne diseases, and also protect against foodborne diseases caused by EHEC. Such recommendations should be implemented in all cases, especially "Cook thoroughly" so that the centre of the food reaches at least 70°C. Make sure to wash fruits and vegetables carefully, especially if they are eaten raw. If possible, vegetables and fruits should be peeled. Vulnerable populations (e.g. small children, the elderly) should avoid the consumption of raw or undercooked meat products, raw milk and products made from raw milk.

Regular hand washing, particularly before food preparation or consumption and after toilet contact, is highly recommended, especially for people who take care of small children, the elderly or immune compromised individuals, as the bacterium can be passed from person to person, as well as through food, water and direct contact with animals.

A number of EHEC infections have been caused by contact with recreational water. Therefore, it is also important to protect such water areas, as well as drinking-water sources, from animal waste.

WHO (2011): Enterohaemorrhagic *Escherichia coli* (EHEC). Symptoms, Electronic source: <http://www.who.int/mediacentre/factsheets/fs125/en/index.html>, last visit: 06.06.2012

## Appendix 2: EHEC and HUS Cases



Source: 2001 - 2009: *Infektionsepidemiologische Jahrbücher des RKI*, 2010-2011: *SurvStat@RKI* (as of 4.11.2011)

### **Appendix 3: The Robert Koch Institute**

#### Tasks and Aims of the Robert Koch Institute

The Robert Koch Institute (RKI) is the central federal institution responsible for disease control and prevention and is therefore the central federal reference institution for both applied and response-orientated research, as well as for the public health sector.

The tasks of the Robert Koch Institute comprise:

The identification of politically important health problems and associated scientific issues

Applied and response-orientated research to resolve these issues

The assessment of scientific results through analysis of current international developments in the respective scientific areas

Informing and advising political decision makers and the scientific sector

Executive tasks defined by special laws, in particular with regard to protection from infection, legislation on stem cell research, and attacks using biological agents

The topical realisation and coordination of federal health reporting.

Apart from the enforcement of special laws, tasks at the RKI include the legal obligation to compile scientific findings as a basis for political decisions concerning health issues. The RKI therefore communicates and cooperates with partners in the scientific sector, the public health service and the health care sector. The institute has major responsibilities in the field of scientific investigation, epidemiologic and medical analysis and evaluation of dangerous diseases, and those with a high prevalence or those of increased public or health-related political significance.

With the passing of the Law for the Prevention of Infection (Infektionsschutzgesetz, IfSG), the RKI was given the responsibilities of a federal epidemiological centre for infectious diseases, combined with the construction of an expert-based registration system, plus other novel and enhanced tools for data generation, prevention, surveillance and research.

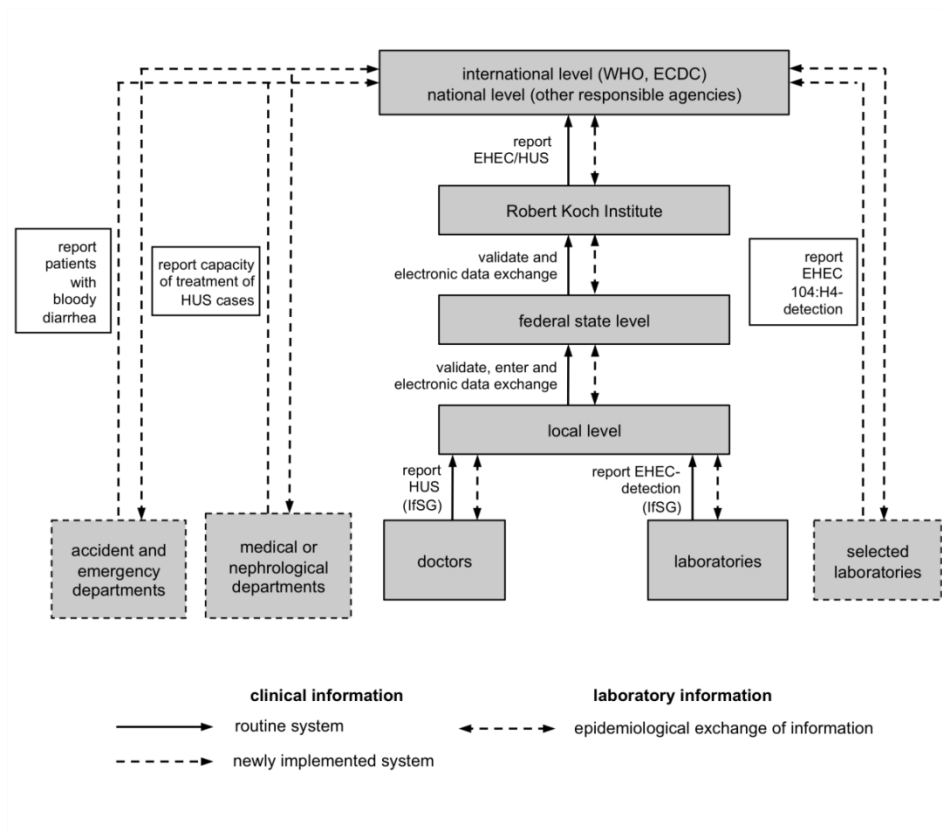
The RKI is responsible for coordinating and carrying out the Federal Health Reporting (Gesundheitsberichterstattung des Bundes, GBE); it is involved in the conceptual design and realisation of epidemiological data collection (in particular survey and sentinel studies), and is concerned with the maintenance and update of the registers and other processed epidemiological data at the federal level. This task is fulfilled in collaboration with the Federal Statistical Office (Statistisches Bundesamt) and other higher federal authorities.

The RKI is further charged with tasks concerning the identification and prevention of attacks using biological agents. To achieve this, the RKI cooperates with civil defence sections at other federal ministries, with federal states, with local authorities, with European and international institutions and with institutions of civil protection, and also informs the scientific sector and the media.

The RKI received further responsibility with the passing of the Stem Cell Law (Stammzellengesetz). This includes the execution of the authorisation procedures based on the Stem Cell Law as well as the maintenance of a register concerning the stem cell lines used and the research approved. The Central Ethics Committee for Stem Cell Research (Zentrale Ethik-Kommission für Stammzellenforschung, ZES) is based at the RKI.

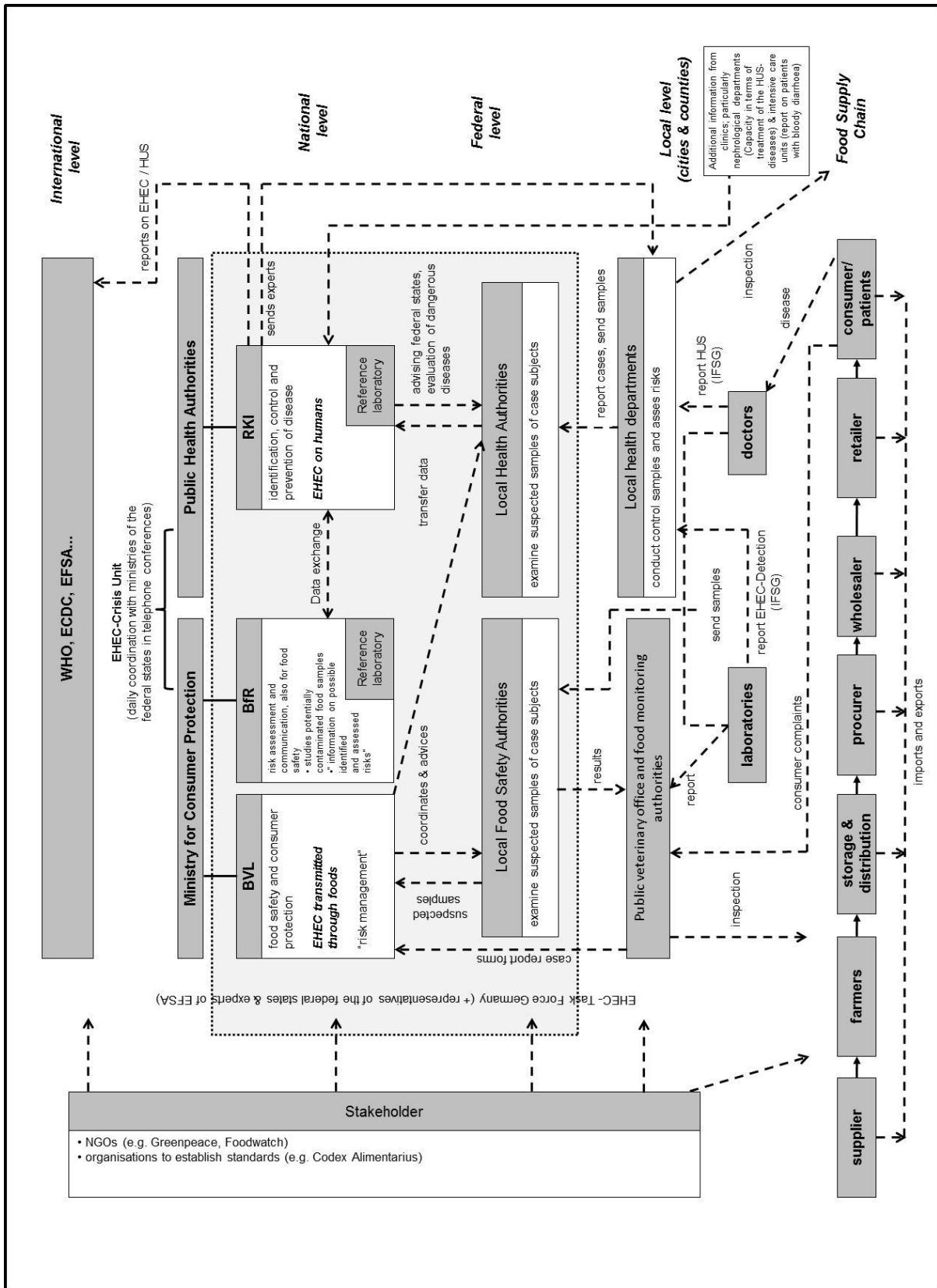
RIKI (2012): Tasks and aims of the Robert Koch Institute. Electronic source: [http://www.rki.de/EN/Content/Institute/General/general\\_node\\_en.html](http://www.rki.de/EN/Content/Institute/General/general_node_en.html), last visit: 06.06.2012

## Appendix 4: Reporting System According to the Prevention of Infection Act in Germany



Source: RKI (2011): Intensivierte Surveillance während eines großen EHEC-/HUS-Ausbruchs in Deutschland, Mai – Juni 2011. *Epidemiologisches Bulletin*. 2011, (15), p. 226.

# Appendix 5: The Fight Against the EHEC Outbreak 2011



Source: Own presentation

## **Appendix 6: Results of the EHEC Task Force**

The German EHEC Task Force was called into action by the Ministry of Food, Agriculture and Consumer Protection (BMELV) to support the food safety side of the EHEC outbreak investigation. Members of the Task Force EHEC were experts from the Federal States (Lower Saxony, Schleswig-Holstein, Mecklenburg-West Pomerania, Hamburg, Bavaria), from the Federal Office of Consumer Protection and Food Safety (BVL), and the Federal Institute of Risk Assessment (BfR). The work of the Task Force was coordinated by the BVL. Additionally, experts from the Robert Koch Institute (RKI) and scientists of the European Food Safety Authority (EFSA) participated in the Task Force.

During the first phase of the outbreak investigation, the main goal was to identify the contaminated food. To achieve this, two different strategies were followed parallel to each other. One approach was a detailed trace back analysis for all salad ingredients and raw vegetables that had been served to customers at five outbreak clusters in order to identify common food sources and delivery chains. The second approach was a trace forward analysis of the supply chains of a shoot producer in order to find out if he had delivered to any outbreak clusters. Both approaches revealed that contaminated shoots from a producer in Lower Saxony were highly likely to have caused the outbreak.

The aim of the second investigation phase was to find and stop the source of the EHEC O104:H4 bacteria. The Task Force gave recommendations on source elimination measures and collected and analysed epidemiological information in order to find out when the source was active. Besides, a detailed trace back for batches of suspicious seeds that had been used by the shoot producer was initiated. The results of this activity formed the basis for the tracing of seeds coordinated by the European Food Safety Authority, which revealed that fenugreek seeds imported from Egypt were the most likely common link between the EHEC O104:H4 outbreaks in Germany and France.

In conclusion, the newly developed outbreak investigation strategy of the Task Force EHEC, with close collaboration between German federal and federal state authorities and between food safety authorities, health authorities and scientists, was a recipe for success and can be a model for future food-borne outbreak investigations.

BVL (2012): Report on the results of the German EHEC Task Force on the EHEC O104:H4 disease outbreak investigation in Germany. Electronic source: [http://www.bvl.bund.de/EN/01\\_Food/06\\_Task\\_Force\\_EHEC/Task\\_Force\\_EN\\_node.html](http://www.bvl.bund.de/EN/01_Food/06_Task_Force_EHEC/Task_Force_EN_node.html), last visit: 06.06.2012

## Appendix 7: Time Flow (own research)

Date	Incident
May 1, 2011	First confirmed EHEC disease (according to RKI - in retrospect)
Early May	According to "Eurosurveillance", the number of EHEC with HUS cases has doubled (as of 9 May)
Beginning second week of May	Seven cases of HUS caused by EHEC (adult women and) and 10-18 new cases a day EHEC (unusual clustering)
May 09, 2011	The BfR warns about eating raw sprouts (current EHEC outbreak is yet unknown), large increase in EHEC cases
Mid-May	Lower Saxony State Office for Consumer Protection and Food Safety identified EHEC toxin (Shiga toxin) on sprout pack
May 16, 2011	According to "Eurosurveillance" new disease climax with 39 HUS cases in one day has been reached
May 19, 2011	RKI learns first official cases of EHEC in UKE Hamburg (due to the long way for notifiable diseases); daily about 60 new cases of HUS and 140 of EHEC
May 20-21, 2011	First exploratory surveys of HUS patients by RKI result in an alert for lettuce, cucumbers, tomatoes (first survey with 12 patients, then case-control study) cooperation with the Federal and regional health and food authorities (BfR press release dated 10.6.)
May 22, 2011	German officials inform the EU through the EWRS system about the EHEC outbreak and classifies it as a "potential public health emergency of international concern within the framework of the International Health Regulations" (cf. Euro Surveillance 16 June, 5)
May 22, 2011	Case-control study by the Robert Koch Institute basis for consumption warnings on May 25)
May 22, 2011	Peak incidence
May 23, 2011	A Situation Centre at the RKI is established as a central operations center (always available), the Robert Koch Institute website provides information on the current EHEC outbreak
May 23, 2011	German Society of Nephrology launches a protected online platform for registration of EHEC cases
May 23-27, 2011	Data from governmental health facilities are mailed daily to the RKI
May 24, 2011	Epidemiological reports are now mailed daily to managers, doctors, laboratories
May 25, 2011	BfR issues consumption warning for suspicious vegetables (cucumbers, lettuce, tomato)
May 25, 2011	RKI asks four laboratories for daily data exchange via email or telephone
May 26, 2011	The Hamburg senator for Health, Cornelia Prüfer-Storcks, and two experts from the Institute for Hygiene and Environment warn of Spanish cucumbers, which were allegedly identified as source of EHEC; Relevant ministries of North Rhine-Westphalia, Baden-Wuerttemberg and Bavaria require safety certificates for the import of Spanish cucumbers
May 26, 2011	Virus strain is identified as HUSEC 41
May 27, 2011	New, non-approved antibiotic is used for the treatment of EHEC patients
May 27, 2011	Surveillance system for patients with and without bloody diarrhea in emergency rooms is implemented (as of June 12, 147 emergency rooms involved)
May 29, 2011	Second study confirmed the RKI result of the first case-control study (triggers were cucumbers, tomatoes and lettuce)



<b>Date</b>	<b>Incident</b>
Approx. May 29, 2011	Closure of two Spanish vegetable production farms
May 30, 2011	From this date onwards: German Society of Nephrology collects data on treatment capacity for HUS patients and sends them to the RKI
May 30, 2011	University of Münster develops an EHEC rapid test for the detection of the pathogen in stool specimens and vegetables
May 31, 2011	BfR and the French Food Safety Agency ANSES develop a specific detection system for EHEC
May 31, 2011	Hamburg Health senator announced that cucumbers are not the source of the current outbreak (Although EHEC was found, but not the type O104: H4)
May 31, 2011	Cucumber, tomato and salad warnings remain; speculation concerning a Lübeck potato cellar shifts into focus the investigators
Early June	In connection with EHEC Russia bans imports of produce from the EU
Early June	Spanish cucumber supplier Frunet takes legal action against the Hamburg authority because of false warnings
June 1, 2011	EU Commission lifts safety warning on cucumbers
June 2, 2011	Genome of the EHEC pathogen can be decrypted (by two different independent research groups)
June 3, 2011	ECDF and EFSA issue health warnings
June 3, 2011	Foundation of EHEC Task Force; First Task Force meeting (definition of outbreak clusters and determination of relevant information)
June 4, 2011	EHEC germ deciphered by a team led by Helge Karch (University of Münster), setting up a nationwide registry to collect outcomes of patients with EHEC
June 5, 2011	EFSA scientists support the EHEC Task Force
June 5, 2011	Minister of Agriculture of Lower Saxony announces that a sprouts farm in Bienenbüttel is suspected; Sprout production is forbidden and the farm decides to cease producing other vegetables as well
June 5, 2011	The opposition criticizes the Ministries for Health and Consumer Protection (Renate Künast)
June 6, 2011	BfR issues warning for sprouts, the RKI follows
June 8, 2011	Employees of the Saxon Ministry of Health discover EHEC on cucumber seeds in Magdeburg
June 8, 2011	EU agriculture commissioner promises financial aid for sheep farmers affected by the outbreak on a meeting of the European ministers of agriculture
June 10, 2011	2nd Meeting of the Task Force: Results from the restaurant-cohort study are available, followed by new consumption recommendations for raw sprouts by BVL, BfR and RKI
June 10, 2011	EHEC is detected in a pack of sprouts in NRW, that comes from Bienenbüttel; number of new cases decreases. BfR, RKI and BVL change dietary recommendations - warning of sprouts (BfR Press Releases 10.06.2011 and 11.06.2011)
June 11, 2011	Authorities raise warning of cucumber, raw tomatoes and lettuce; still warning of sprouts (Robert Koch Institute, the Federal Institute of Risk Assessment, Federal Office for Consumer Protection and Food Safety)
June 12, 2011	BfR warns of eating raw home-grown sprouts and seedlings
June 13, 2011	In Bavaria EHEC pathogens are found on lettuce, but the type is still unknown
June 13, 2011	Task Force presents the first results: 41 outbreak clusters were supplied with sprouts from the sprout farm in Bienenbüttel
June 14, 2011	EU Commission announces compensation payments of € 210 million for European farmers
June 15, 2011	Scientists at the University of Göttingen decrypt information of E. coli O104: H4
June 16, 2011	EHEC Rapid Test that detects the infection in less than two hours is available (usually 24-36h)
June 17, 2011	EHEC pathogen is detected in Bach near Frankfurt (but not pathogen O104: H4)
June 19, 2011	Retailers also call for compensations
June 22, 2011	EHEC outbreak reported in France (8 cases, probably same pathogen as in Germany)
June 25, 2011	EHEC O104 pathogens: H4 cannot be detected in Bach near Frankfurt
June 27, 2011	In the county of Paderborn a school is closed due to several EHEC cases in one week
June 28, 2011	EHEC pathogen O104:H4 is reported in Sweden
June 28, 2011	Russia raises the ban on imports from the EU (though initially only from certain countries)
June 30, 2011	Fenugreek seeds from Egypt are suspected as the cause of the epidemic EHEC (according to EFSA, ECDC and BfR)
July 4, 2011	EHEC-mass test is started in the county of Paderborn (due to the school closures due to EHEC)

Date	Incident
July 5, 2011	EU releases import ban on certain seeds and beans (in any case, fenugreek seeds and soybeans) from Egypt and recall batches of seeds. Problem: Disease-causing shoots were already imported to Germany in 2009. For products that contain the seeds no recall or similar action is initiated.
July 8, 2011	Medicine containing fenugreek seeds (between 2009 and 2011, imported from Egypt), are being recalled from the German market
July 15, 2011	The farm in Bienenbüttel may produce again
July 27, 2011	The Robert Koch Institute announces officially that the EHEC outbreak is over
August 1, 2011	Tax exemptions are granted for farmers in need
August 3, 2011	Federal government announces to turn the EHEC Task Force into a permanent organization ("Special commission")
Early August	EU expert team travels to Cairo in order to clarify the EHEC outbreak - visit is postponed till September the earliest because of disagreements about the team's work between Brussels and Cairo
August 30, 2011	EU expert team reports that no EHEC contaminated sprouts were identified, resulting in a possible lift of the ban on Egyptian seed
August 31, 2011	A draft for shorter notification times to the Robert Koch Institute for EHEC/HUS related infections is introduced