both neurons and glial cells (e.g., oligodendrocytes and astrocytes). One particular cell line, known as NSI-566RSC, has been cultured for use with ALS treatment.[12] These cells have been transplanted into the lumbar spinal cord of ALS-affected mice; encouragingly, this resulted in motor function being retained for longer, and lifespan was extended by up to 12 days, compared to control mice.[13] If NSI-556RSC cells are transplanted into the cervical spinal cord as well as lumbar spine, lifespan is increased to 17 days.[14] It is thought that the reason for this improvement is the increase in neurotrophic factors that occurs post-transplantation.[13] A phase I US Food and Drug Administration (FDA)-approved trial is currently ongoing (ClinicalTrials.gov identifier: NCT01348451) transplanting the NSU-556RSC cell line (sourced from human spinal cord) into the spinal cord of ALS patients; final results are expected in December 2015. Initial findings show that this procedure can be well tolerated and there is even evidence to suggest the progression of ALS is slowing.[15]

In conclusion, stem cells show potential to be used in the treatment of ALS, as shown by the animal and human studies outlined above. Ethical and legislative barriers are arguably more difficult to overcome than the scientific techniques underpinning these therapies; however, this is not unusual in the field of stem cell research. Unfortunately, the data that have been published to date cannot be used to show conclusive evidence that stem cell therapy produces a significant effect in slowing or reversing the effects of ALS. It would now be useful for a large-scale trial to be carried out as current sample sizes are very small. The introduction of blinding the study and using a placebo has been suggested; however, this could result in control patients having high-risk surgical procedures (e.g., the surgical exposure of the spinal cord). Owing to the debilitating nature of ALS, even minor improvements to an individual's situation are desirable and can result in a much improved perceived quality of life. Stem cell therapies may be the best potential method of achieving such a result.

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Investigation into the misidentification of Hazard Group 3 gastrointestinal pathogens and associated health and safety risks

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The Gastrointestinal Bacteria Reference Unit (GBRU) at Colindale, London, receives isolates from a network of frontline local hospital and Public Health England (PHE) laboratories in England and Wales for confirmation of identification and typing, for purposes of surveillance and outbreak investigation. Many gastrointestinal (GI) pathogens are zoonotic and/or foodborne and investigations at GBRU enable PHE to monitor the safety of food and the environment.[1,2] Certain GI pathogens, notably *Salmonella enterica* subspecies *enterica* serovar Typhi (*S.* Typhi), *Salmonella enterica* subspecies *enterica* serovar Paratyphi (*S.* Paratyphi) and verocytotoxin-producing *Escherichia coli* (VTEC) cause severe disease that can be fatal.[3,4]

In England, the frontline microbiology laboratories isolate GI pathogens from faecal specimens from symptomatic cases using selective media and identify the species by performing biochemical tests and serology.[5] In recent years, automated identification platforms, such as Phoenix, VITEK and matrix-assisted laser desorption/ionisation-time of flight mass spectrometry (MALDI-TOF MS) have emerged as rapid, cost-effective methods of identifying pathogens in diagnostic microbiology laboratories.[6] Although these platforms reduce the turnaround times for identification of bacterial species, they lack discrimination in some areas.

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Table 1. *Salmonella* serovars submitted to the Gastrointestinal Bacteriology Reference Unit (GBRU) from 1 January 2010 to 28 February 2014 and the Hazard Group (HG) as indicated on the request form.*

	HG3	HG2	Total
Salmonella Typhi	1,230	3	1233
Salmonella Paratyphi A	909	0	909
Salmonella Paratyphi B	59	9	68
Salmonella Paratyphi C	2	0	2
Total *S.* Typhi or *S.* Paratyphi	2200	12	2,212
Non-typhoidal *Salmonella*	6362	33,962	40,324
Total	8562	33,974	42,536

*In addition, two isolates of *Shigella* sp. submitted as HG2 were subsequently identified as *S.* Typhi.

Introduction of novel methods has led to a reduction in the use of more traditional modes of identification such as serological agglutination methods, thus reducing the technical interpretation of results and consequent loss of technical knowledge and skill over time.

Since 2010, there has been an increase in the number of misidentified *S.* Typhi, *S.* Paratyphi and VTEC isolates submitted to GBRU as Hazard Group 2 (HG2) pathogens, thus increasing the risk of exposure of staff, both in frontline and reference laboratories, to Hazard Group 3 (HG3) organisms.[7]

The purpose of this brief report is to summarise the number and type of misidentified HG3 cultures submitted to GBRU as HG2 pathogens, highlight the health and safety implications and recommend actions to reduce the risks.

Between January 2010 and February 2014, 12 isolates of *Salmonella* spp. and two isolates of *Shigella* spp. submitted to GBRU as HG2, were subsequently identified as *S.* Typhi or *S.* Paratyphi (Table 1). Follow-up investigations implicated the use of novel automated identification platforms used by frontline laboratories. Certain protocols identified these clinically significant isolates incorrectly at the species level, while other protocols identified the pathogens to the genus *Salmonella* only. The use of the automated identification platforms to identify *Salmonella* at the species and subspecies level has been evaluated; however, the clinically important serovars, *S.* Typhi and *S.* Paratyphi were either not included, or not adequately represented, in these studies.[8]

Since 2010, 14 VTEC were submitted as HG2 *Shigella* or *Salmonella* spp. but were proactively identified as potential VTEC and processed at HG3. *E. coli* and *Shigella* spp. are notoriously difficult to differentiate by the tests available at the frontline laboratories. Strains of *E. coli* that most closely resemble *Shigella* spp. are often pathogenic and capable of causing GI disease.[9] A recently emerged strain of VTEC serotype O117 is similar biochemically to *S. sonnei* and the majority of the misidentifications highlighted in Table 2 are associated with this emerging pathogen.[10]

Exposure of laboratory staff to an HG3 pathogen at Containment Level 2 is regarded by the Health and Safety Executive (HSE) in the UK as a dangerous occurrence and should be reported to the HSE following the guidance on Reporting of Injuries, Diseases and Dangerous Occurrences Regulations (RIDDOR).[11]

The misidentification of HG3 cultures at frontline microbiology laboratories may increase the risk of exposure of the public to these pathogens due to inappropriate public health action; for example, failure to exclude a food handler from work.

In 2010, GBRU implemented guidance to its staff for the identification of potential cultures of *S.* Typhi and *S.* Paratyphi submitted by frontline laboratories as HG2 *Salmonella* spp. Of the 12 isolates described above and in Table 1, 10 were processed at HG3 as they were classed as being potential HG3 pathogens using the following guidelines: i) those isolates from blood; ii) isolates from cases with symptoms of fever, septicaemia, rigor or pyrexia of unknown origin; and iii) isolates from cases who report travel to an endemic region. Where the details supplied by the sending laboratory were insufficient to determine the hazard group, every effort was made to establish the correct hazard group by contacting the sender to clarify findings, such as the methods used to identify the pathogen. While these measures have had the desired effect in capturing misidentified isolates, the subsequent increase in CL3 workload has affected the turnaround time at the reference laboratory for identification.

The GBRU processes all cultures identified as HG2 *Shigella* spp. by the frontline diagnostic laboratories at HG3, where the sender reports that the culture was negative for *Shigella* agglutinations or where no serology result is provided. There is a requirement for colleagues at the frontline laboratories to document any agglutination reactions determined and to state the methods used to identify the organism on the specimen request form submitted to GBRU with the culture. The specimen request form also includes a statement warning that a negative agglutination result with *Shigella* antisera may indicate the detection of a strain of atypical VTEC.

Laboratory processes at GBRU have been re-engineered so that polymerase chain reactions (PCRs) to differentiate VTEC and *Shigella* species are carried out before processing any cultures at HG2. This algorithm identifies potential HG3 isolates that have no HG3 indicating factors on the specimen request form.

Colleagues at GBRU continue to liaise closely with manufacturers and colleagues at frontline microbiology laboratories to improve awareness regarding best practice. Laboratory workers should ensure that novel approaches to

Table 2. Verocytotoxogenic (VT) status and the Hazard Group (HG) as indicated on the request forms of the isolates sent to GBRU from 1 January 2010 to 28 February 2014.

	Isolates submitted to GBRU as HG2 isolates		Isolates submitted to GBRU as HG3		
Year	VT-positive	Non-VT	VT-positive	Non-VT	Total
2010	0	2515	980	421	3919
2011	4	2340	1365	308	4018
2012	2	2031	1180	358	3576
2013	5	2479	1055	499	4053
2014	3	352	112	101	566
Total	14	9717	4692	1687	16,132

VT: verocytotoxogenic or *Shiga* toxin producers.

laboratory practice have been fully assessed and are regularly audited. Newly implemented protocols must be fully validated and clinically evaluated. Colleagues in GBRU are working with colleagues in industry to create a more comprehensive database for the Enterobacteriaceae, including *S.* Typhi and *S.* Paratyphi, *Shigella* spp. and emerging or unusual strains. A careful balance needs to be maintained by frontline laboratories between the advantages of new technology and the safety associated with more traditional methodology until databases of novel methods are fully evolved.

Maria Zambon highlighted the necessity of producing this rapid communication. Steve Connell and Marie Chattaway conducted the investigation, and David Powell extracted the data from the laboratory records. All authors contributed to the analysis and presentation of the data and drafted and approved the final manuscript.

The authors would like to thank Professor Maria Zambon for invaluable advice and support, Dr. Lakshani Rajakaruna for technical advice and direction, and the sending laboratories for their contribution to the investigation.

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