before thalidomide determination. The recent reports they cite used two strategies to minimize specimen degradation: acidification and rapid cooling, either alone or in combination. All authors agree that special handling is required.

Contrary to the Eriksson et al. study with rat blood [1], our previous report [2] did not recommend dilution of whole-blood specimens with acidic buffer for human clinical trials for several reasons:

1) Our study addressed the assay of plasma thalidomide. In our experience, mixing blood and acidic buffers promoted hemolysis, which increased the variability in thalidomide recovery from plasma. Our study demonstrated that acidification of plasma to pH 6.0 did not stabilize thalidomide at −25 °C; consequently, we advocated that frozen specimens be analyzed within 1 month to minimize degradation.

2) In multicenter clinical trials, specimen collection frequently occurs in an area away from the laboratory, resulting in delays before specimen centrifugation or handling. To immediately reduce the degradation of thalidomide, we advocate rapidly cooling specimens in icewaterbefore transporting the blood specimen to the laboratory for centrifugation and frozen storage.

If a clinical trial requires the measurement of whole-blood thalidomide, immediate acidification of whole blood could be accomplished by collecting blood into evacuated test tubes already containing a volume of acidic buffer. Partial filling of the test tubes in this approach would lead to variability in the blood:buffer ratio, a source of preanalytical variation. Eriksson and Björkman suggest mixing equal volumes of blood and buffer in the laboratory. This acidification method would be accurate and precise but would necessitate immediate processing to avoid the loss of as much as 4% of the thalidomide within 15 min, as they have noted.

3) Acidification to pH <6.0 may offer long-term aqueous thalidomide stability. Clearly, our study [2] and that of Eriksson et al. [1] demonstrate the instability of thalidomide in plasma at −25 °C at pH 6.0 or pH 7.4, respectively. Boughton et al. demonstrate that acidification improves short-term stability [3]. Contrary to earlier reports suggesting that aqueous thalidomide is stable at pH 6.0 [4, 5], we agree with Eriksson and Björkman’s suggestion that a pH <6.0 may be required to confer stability.

Eriksson and Björkman’s statement above that whole-blood thalidomide specimens at pH 5.1 and −25 °C have long-term stability is important. In our opinion, it suggests that a combination of rapid specimen cooling and prompt acidification to pH 5.1 (or less) and frozen storage of the blood or plasma could provide for both short-term and long-term stability and allow for longer intervals between specimen collection and thalidomide determination in clinical trials.

References

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Nonisotopic Method for Precise Detection of (CAG)n Repeats

To the Editor:
Muglia et al. [1] recently reported a sensitive method for silver nitrate staining of PCR products separated by polyacrylamide gel electrophoresis for the diagnosis of Huntington disease. We use silver staining [2] of PCR products to detect expanded CAG trinucleotide repeats in other diseases as well, specifically, spinal bulbar muscular atrophy (expanded repeat length range 40–62), spinal cerebellar ataxia type I (40–82), and dentatorubral-pallidoluysian atrophy (49–75). The primers and PCR reaction mixtures described by Watkins et al. [3] can be used with the following thermal conditions for each gene amplification: 2 min of denaturation at 96 °C; followed by 30 cycles of 96 °C for 1 min, 62 °C for 1 min, and 72 °C for 1 min; and finally 10 min at 72 °C for final extension. For more-accurate sizing of PCR products on the gel, we use a 50-bp ladder from Pharmacia (Uppsala, Sweden; cat. no. 27–4005). In view of the need for precise diagnostics procedures for the dynamic trinucleotide repeat expansions [4], we recommend using these easy methods.

References

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Undisclosed Radioactivity in Specimens: How Much of a Problem?

To the Editor:

Our institution, a clinical reference laboratory, receives specimens from a wide geographic location. In September 1996, a waste-disposal contractor alerted us to the presence of residual radioactivity in a 30-gallon (~135-L) drum of what was supposed to be nonradioactive laboratory waste. Because clinical laboratories are regulated regarding the receipt, use, and disposal of radioactive material, we sought the source. Investigation revealed that the radiation originated from a urine specimen container, specifically from a specimen sent for catecholamine testing. During an evaluation for a possible pheochromocytoma, the patient involved had undergone nuclear imaging with radiolabeled m-iodobenzyl guanidine (MIBG) before urine collection for biochemical studies (MIBG is often used in nuclear medicine to evaluate suspected pheochromocytomas [1]). The isotope involved was 131I, which has an 8-day half-life. In spite of the short half-life, residual radioactivity was detected >30 days after the isotope’s arrival in the laboratory.

After considering the implications of this case, we began to screen for radioactivity specimens received for catecholamine analysis, because this group included patients who were likely to be evaluated with nuclear imaging procedures. Initial screening was performed with a hand-held radiation monitor (TBM-6SP; Technical Associates, Canoga Park, CA), and those specimens identified as radioactive were quantified with a gamma counter (Genesys 6000; Laboratory Technologies, Roselle, IL). Between October and January, ~1% of the specimens screened (8 of 928) were found to be radioactive. These specimens had been received from multiple locations and contained between 0.2 and 1160 μCi/L. Total radioactivity in a single 24-h collection was as much as 0.4 mCi. The health risks to laboratory personnel from inadvertent exposure to the low amounts of radiation described here are minimal. However, associated regulatory and licensing issues are of considerable concern.

Low-level radioactive waste issues are discussed in references such as Hill [2]. Nuclear Regulatory Commission (NRC) regulation 10 CFR 20.2003(b) states that excreta from individuals undergoing medical diagnosis or therapy with radioactive materials are exempt from regulation if discharged directly into the sanitary sewer. However, the subject of radioactive specimens forwarded to the clinical laboratory is not commonly addressed in the literature, particularly specimens containing undisclosed radiation and shipped to distant laboratories. Regulations concerning laboratories vary widely by state and by type of licensure. Many states are licensed directly through the NRC. In our case, the laboratory has a “radioactive material license” from the State of Utah, which allows the presence of several radionuclides on site, including 131I, up to a total of 3 mCi. Licenses do not necessarily include 131I, and each laboratory experiencing problems similar to that described here needs to determine what is allowed under its specific licensing regulations. Analysis of low-level radioactive specimens is permissible as long as the amounts are in compliance with licensing regulations. Liquid specimens containing low-level radioactivity can be discarded into the sewer, but the containers should be considered solid radioactive waste and treated accordingly (10 CFR 20.2003). Decay in storage is an authorized method for radioactive waste disposal.

A separate issue involves Department of Transportation (DOT) regulations concerning shipment of radioactive materials. If patients’ specimens are included under DOT regulations concerning shipment of “limited quantities” of radioactive materials (specifically 49 CFR 173.421 and related paragraphs), then certain conditions must be met, including appropriate packaging and minimal labeling requirements [3]. Above specified radiation values, more-stringent packaging and labeling requirements apply.

A number of questions remain, although clearly, undisclosed radiation has the potential to be a significant problem for the clinical laboratory. When a radioactive specimen is discovered, the laboratory needs to verify that it is licensed to have radioactive material of that nature on-site. Clinical laboratories should be aware that specimens are shipped from patients who have undergone nuclear medicine procedures; these specimens may contain undisclosed low-level radiation, which may cause problems with waste disposal and related regulatory policies.

References


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Rapid Qualitative TSH Test to Screen for Primary Hypothyroidism

To the Editor:

We evaluated a qualitative, solid-phase two-site immunochromato-

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