

# Applications in Contrast Imaging

## Clinical Utility of Barium Sulfate Products: Formulation Determines Appropriate Use

*Steven Sireci, MD*

Supported by an educational grant from  
Bracco Diagnostics, Inc.

# CE Information

## Clinical Utility of Barium Sulfate Products: Formulation Determines Appropriate Use

### Summary

Barium-containing contrast media contain barium sulfate ( $\text{BaSO}_4$ ), as well as a number of additives. The  $\text{BaSO}_4$  provides radiodensity (ie, radio-opacity) and physical density (g/mL) to the suspension. Depending on the intended use of the contrast, the specific combination of additives provide other useful properties, including:  $\text{BaSO}_4$  particle suspension; mucosal coating; viscosity and texture; sweetness; filling and laxative effects; preservation; foaming prevention; and flavoring. Here we describe the purpose of each ingredient and additive found in  $\text{BaSO}_4$  contrast media products currently available for fluoroscopic and radiographic examinations. In addition, we review the role of these products in anatomic radiographic evaluation of the gastrointestinal (GI) tract and in evaluation of the physiology of swallowing. Finally, we review barium preparations used in computed tomography (CT) applications.

### Learning Objectives

At the conclusion of this activity, participants should be able to:

- Explain the role that  $\text{BaSO}_4$  plays in barium-containing contrast media;
- Review the purpose of each ingredient/additive found in  $\text{BaSO}_4$  contrast media products available for fluoroscopic and radiographic examinations;
- Describe the formulation of barium products that are appropriate for single- and double-contrast anatomic radiographic evaluation of the gastrointestinal (GI) tract;
- Summarize qualities of the barium-containing contrast media used in evaluation of swallowing that make them most appropriate for that application; and,
- State the properties of barium-containing contrast media used in computed tomography (CT) applications.

### Author



**Steven Sireci, MD**, is Head of Medical Services – Americas, Global Medical & Regulatory Affairs, Bracco Diagnostics Inc., Monroe Township, NJ, USA.

*Financial disclosure for Dr. Sireci includes: Employee of Bracco Diagnostics, Inc., which manufactures barium sulfate products for diagnostic imaging. He has no non-financial relationships to disclose*

### Obtaining Credits

#### Instructions

To earn CE credit, participants must complete this activity during the accreditation period and follow these instructions.

1. Review this article in its entirety.
2. Visit [appliedradiology.org/aici](http://appliedradiology.org/aici).
3. Login or create an account.
4. Add activity to your account.
5. Complete the post test.
6. Complete the evaluation.
7. Print your certificate.

#### Accreditation Period

Release: July 1, 2021

Renewal Expiration: July 31, 2026

#### Accreditation

This article confers 0.75 ARRT Category A Continuing Education credit, which will be awarded upon completion of an online post test. The entire text of this supplement, learning objectives, and the post test are available at [appliedradiology.org/aici](http://appliedradiology.org/aici).

#### Commercial Support

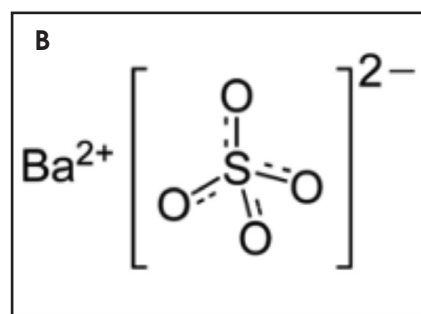
This program was supported through an educational grant from Bracco Diagnostics, Inc.

# Clinical Utility of Barium Sulfate Products: Formulation Determines Appropriate Use

**B**arium (Ba) is an alkaline earth metal found in the second column of the periodic table.<sup>1</sup> In pure form, it is a soft, silvery-white metal with a slight golden shade.<sup>1</sup> Based on its atomic number (56), barium is excellent for blocking X-rays of the energies used in medical imaging. However, barium is too reactive to exist as a pure metal in nature<sup>1</sup> and, therefore, cannot be administered in pure form for the purposes of medical imaging.

Barium sulfate ( $\text{BaSO}_4$ ) is a common, stable, inorganic, insoluble mineral salt, used industrially as a filler for rubber, plastics, and resins<sup>2</sup> (Figure 1). Although difficult to dissolve in water,  $\text{BaSO}_4$  can be suspended in water with the help of additives, providing radiodensity (ie, radio-opacity) and physical density (g/mL) to the suspension. Concentrated suspensions ranging from 40% up to 240% weight-to-volume (w/v) can be used in fluoroscopy and radiography for a variety of clinical applications. To use  $\text{BaSO}_4$  for computed tomography (CT), a technology that has a very exquisite discrimination of radiodensities, the suspension has to be greatly diluted, to approximately 2% w/v. Preparations in that low concentration range are made and sold for several specialized abdominal CT imaging procedures.

In addition to  $\text{BaSO}_4$ , barium-containing contrast media have a number of additional ingredients (almost all common food additives) that provide the important physicochemical properties of each product. Here we describe the purpose of each ingredient/additive found in  $\text{BaSO}_4$  contrast media products currently available for fluoroscopic and radiographic examinations. In addition, we review the role of these barium products in both the anatomic radiographic evaluation of the gastrointestinal (GI)



**FIGURE 1.** (A) Barium sulfate salt; (B) barium sulfate chemical formula.

tract and in evaluation of the physiology of swallowing. Finally, we review barium preparations used in CT applications.

## Barium Sulfate Formulations for Radiographic Procedures

$\text{BaSO}_4$  itself is inert and not absorbed from the GI tract. It is present in contrast media to provide radio-opacity, which is determined by the  $\text{BaSO}_4$  concentration, and physical density. It has no pharmacologic effects, nor can it cause an allergic reaction. However, if  $\text{BaSO}_4$  leaks from the GI lumen, it can cause mediastinitis, peritonitis, or retroperitonitis.<sup>3</sup> Importantly, these adverse clinical events result from a severe granulomatous reaction,<sup>4</sup> and therefore are distinct from the concepts of both “hypersensitivity” and “toxicity.”

Additives present in  $\text{BaSO}_4$  contrast media formulations include emulsifiers, stabilizers, and dispersants to keep the  $\text{BaSO}_4$  particles smoothly suspended in water, without which the  $\text{BaSO}_4$  particles would simply sink to the bottom and clump. Mucosal-coating thickeners provide stickiness, while non-coating thickeners increase viscosity. Inclusion/exclusion of such thickeners is essential, as mucosal coating is vital for some applications (eg, double-contrast GI imaging), while detrimental to others (eg,

modified barium swallow study [MBSS] to evaluate swallowing physiology, in which precise viscosities are critical). Finally, additives are included to ensure that  $\text{BaSO}_4$  products are palatable, readily eliminated, non-foaming, and long-lasting. Here we review the additives that provide each of these properties, to provide a better understanding of how they contribute to clinical utility of the various barium-containing contrast media (Tables 1 and 2).

## Emulsifiers/Stabilizers/Dispersants

Since  $\text{BaSO}_4$  is not soluble in water, in order for it to be used as a contrast medium, emulsifiers, stabilizers, and dispersants must be added to maintain smooth  $\text{BaSO}_4$  particle suspension, along with pH regulators to maintain suspension efficacy. One of these is carboxymethyl-cellulose sodium, a negatively charged polymer that coats  $\text{BaSO}_4$  particles. At low concentrations, carboxymethyl-cellulose sodium helps to suspend the particles in water via electrostatic repulsion. Other emulsifiers/stabilizers/dispersants include sodium citrate, a dispersant that also helps regulate pH, and polysorbate 80, a surfactant that also is anti-foaming. These 3 multi-purpose additives are present in many  $\text{BaSO}_4$  preparations.

**Table 1. Properties and Ingredients of Barium Products Used for Anatomic Procedures**

<b>BaSO<sub>4</sub> CONCENTRATION</b>	<b>SC UGI</b> ~60% w/v	<b>SC UGI (powder)</b> ~60-120% w/v	<b>DC UGI (powder)</b> ~240% w/v	<b>SMALL BOWEL</b> ~25% w/v	<b>BARIUM ENEMAS</b> DC: ~100% w/v SC: ~50% w/v	<b>PASTE (for esophagus or rectum)</b> ~60% w/w
<b>EMULSIFIERS/STABILIZERS/DISPERSANTS</b>						
Carboxymethyl-cellulose (low conc.)	X					
Sodium citrate	X	X	X	X	X	X
Polysorbate 80	X	X	X	X	X	
<b>MUCOSAL COATING/THICKENERS</b>						
Acacia gum			X	X	X	
Tragacanth gum		X				
Carboxymethyl-cellulose (high conc.)						X
<b>NON-COATING THICKENERS</b>						
Xanthan gum	X	X		X	X	
Carrageenan		X	X	X	X	
Pectin		X				
Methylcellulose				X		
<b>SWEETENERS/TEXTURIZERS</b>						
Glycerin						X
<b>SWEETENERS/LAXATIVES</b>						
Sorbitol	X	X	X	X	X	X
<b>SOLVENT</b>						
Propylene glycol		X				
<b>OTHERS</b>						
Preservatives	X			X	X	X

Conc.=concentration; DC=double contrast; SC=single contrast; UGI=upper gastrointestinal; w/v=weight/volume.

**Table 2. Properties and Ingredients of Barium Products Used for MBSS**

<b>BaSO<sub>4</sub> CONCENTRATION</b>	<b>THIN LIQUID (powder)</b> 40% w/v reconstituted	<b>NECTAR</b> 40% w/v	<b>THIN HONEY</b> 40% w/v	<b>HONEY</b> 40% w/v	<b>PUDDING</b> 40% w/v
<b>VISCOSITY (cPs)</b>	<15	300	1500	3000	5000
<b>EMULSIFIERS/STABILIZERS/DISPERSANTS</b>					
Carboxymethyl-cellulose (low conc.)	X	X	X	X	
Sodium citrate	X	X	X	X	
Polysorbate 80	X	X	X	X	X
<b>NON-COATING THICKENERS</b>					
Xanthan gum		X	X	X	X
Carboxymethyl-cellulose (medium conc.)					X
Modified corn starch			X	X	
<b>SWEETENERS/TEXTURIZERS</b>					
Glycerin		X	X	X	X
Maltodextrin	X	X			X
<b>SWEETENERS/LAXATIVES</b>					
Xylitol	X	X	X	X	X
Sorbitol	X				
<b>OTHERS</b>					
Preservatives		X	X	X	X

Conc.=concentration; cPs=centipoise; MBSS=modified barium swallow study.



### **Mucosal-coating and Non-coating Thickeners**

Mucosal coating is achieved by increasing the stickiness of the barium product. Additives that increase stickiness include the plant saps acacia gum (aka, gum arabic, the sap of the acacia tree) and, to a lesser degree, tragacanth gum (the sap of the astragalus gummifer shrub). Electrostatic forces can also provide mucosal coating, and this can be achieved by adding high concentrations of carboxymethyl-cellulose sodium. These additives also perform more than one role: all 3 serve as thickeners, increasing viscosity; acacia gum and carboxymethyl-cellulose help suspend the BaSO<sub>4</sub> particles.

Non-coating thickeners increase viscosity, but not stickiness, of the barium product; therefore, they do not result in mucosal coating. Products containing non-coating thickeners are suitable for the MBSS and single-contrast anatomic imaging, for which mucosal coating is undesirable. Non-coating thickeners include xanthan gum, a bacterial polysaccharide; carrageenan, a sulfated polysaccharide from red seaweed; pectin, a heteropolysaccharide from plant cell walls; modified corn starch (which is also anti-sticking/anti-caking), and methylcellulose, which are plant-fiber molecules bound to -CH<sub>3</sub> moieties. Unlike the broader ranges of viscosity acceptable in anatomic imaging of the GI tract, the viscosities of the barium products used in the MBSS are tightly controlled and highly standardized, with increasing amounts of non-sticky thickeners present in correspondingly more viscous preparations.

### **Sweeteners/Texturizers/Laxatives**

BaSO<sub>4</sub> contrast agents should be palatable; thus, they require sweeteners, such as glycerin (aka, glycerol, a polyol), maltodextrin (a variable short-chain polysaccharide of glucose), and xylitol and sorbitol (poorly digestible sugar alcohols). Of note, such sweeteners play other important roles. Xylitol and sorbitol are also osmotic laxatives that hold water in the bowel, maintaining suspen-

sion and speeding transit time through the GI tract; at least one of them will be found in all BaSO<sub>4</sub> preparations. Sweeteners can also act as texturizers and/or thickeners, creating a food-like texture ("mouthfeel") and increasing viscosity. Glycerol also functions as a surfactant.

### **Others**

Other important additives include: anti-foaming agents, such as simethicone and polysorbate 80, to ensure that the product doesn't get bubbly when shaken; pH regulators, including citric acid, sodium citrate, HCl, and KCl, to maintain proper acid/base balance for successful suspension; and preservatives such as sodium benzoate, potassium sorbate, methylparaben, and propylparaben to increase the shelf life of liquid BaSO<sub>4</sub> preparations.

Preservatives are not added to powdered BaSO<sub>4</sub> preparations, which should be used shortly after reconstitution, based on manufacturer's recommendations. Further additives include flavorants such as ethyl maltol, ethyl vanillin, natural/artificial fruit flavors, and saccharin, and the nontoxic solvent propylene glycol to help mix a powdered preparation with water.

### **Imaging with BaSO<sub>4</sub> Preparations** **Anatomic Radiographic** **Evaluation of the GI Tract**

Anatomic evaluation of the GI tract with barium products includes single- and double-contrast upper GI (UGI) examinations (esophagus, stomach, and duodenum), as well as evaluation of the small bowel, colon, and rectum (Figure 2). The purpose of these exams is to identify and characterize anatomic lesions such as tumor, inflammation, obstruction, malformation, and others with an opacifying contrast agent that can either coat or fill the lumen. BaSO<sub>4</sub> products used for all these applications must have high physical and radiographic density, ranging from 24% to 240% w/v.

Double-contrast UGI imaging is used to reveal detail of the GI tract's mucosal inner lining to reveal ulcers, polyps, inflammatory patterns, etc. In

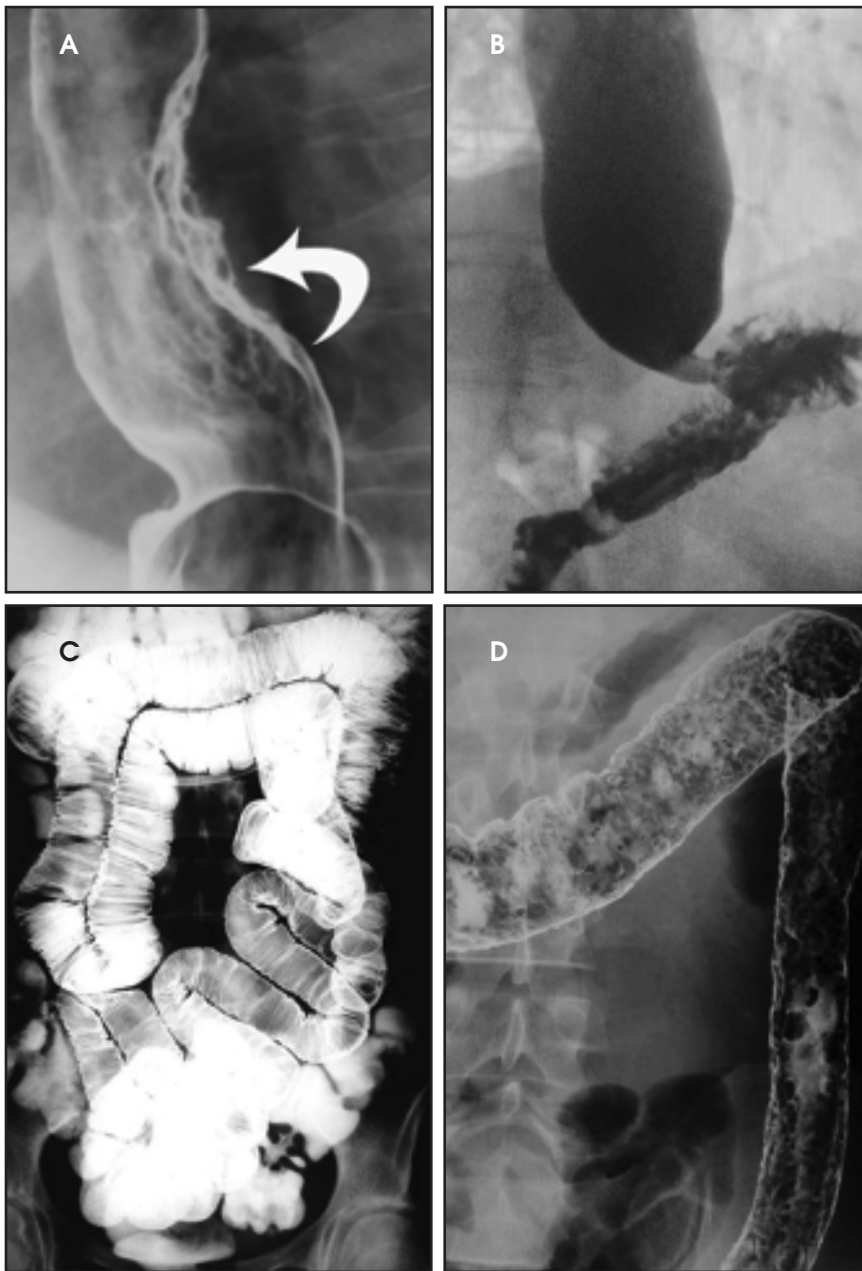
order to see these structures, the mucosal lining must get a thin, even coating of a high-density, sticky BaSO<sub>4</sub> preparation while the lumen is filled with air or gas. (Table 1) Therefore, the BaSO<sub>4</sub> contrast agent must contain a sticky gum (eg, acacia gum) for mucosal coating, and be highly radiodense (100-240% w/v).

On the other hand, single-contrast upper GI imaging is used to see general anatomy and anatomic lesions. The GI structures must be filled with contrast, which is typically not problematic in AP or mildly oblique projections, owing to relatively little overlapping of upper GI structures in those projections. Therefore, for this exam, the lumen must be filled with a well-mixed, moderate-density (60-120% w/v) solution of a non-sticky (ie, no sticky gums) BaSO<sub>4</sub> preparation.

Small bowel follow-through (SBFT) examination or enteroclysis (direct contrast administration into the small bowel) can be done as a single- or double-contrast procedure. The main challenge is to fill and "see through" a long stretch of heavily overlapped bowel loops. So, the barium contrast must provide significant substance and should be of relatively low concentration. In addition, some mucosal coating may be helpful. Therefore, the formulation should consist of non-sticky thickeners/fillers (such as methylcellulose, xanthan, or carrageenan) and a small amount of sticky gum, and be of low radiodensity (<25% w/v).

For a double-contrast barium enema, the anatomic consideration is capacious bowel loops with some overlapping, especially on oblique views of the sigmoid and splenic flexures. The primary barium contrast requirement is mucosal coating (filling is achieved with insufflated air); however, too much stickiness may interfere with instilling the coating all the way to the cecum. Therefore, the barium preparation has a moderate concentration of sticky gum, and a moderate radiodensity (100% w/v).

For the single-contrast barium enema, filling is the priority, and overlapping loops can be a considerable



**FIGURE 2.** Representative images from (A) a double-contrast upper gastrointestinal (UGI) examination (Image previously published in: Iyer R et al. *Cancer Imaging*. 2004;4:125-132.); (B) a single-contrast UGI examination (Image courtesy of: Jo Ann Puntill-Sheltman, SLP, Intermountain St. George Regional Hospital, UT); (C) a small-bowel follow-through (SBFT) examination (Image courtesy of: Marc S. Levine, MD), and (D) a double-contrast barium enema (Image previously published in: Baldwin M et al. *Appl Radiol*. 2012;41: 29-35.)

problem. The barium preparation should have non-sticky thickeners and fillers such as xanthan or carrageenan, and low radiodensity (50% w/v).

When performing defecography, the primary anatomic consideration is that the rectum may be capacious, and therefore, the radiodensity should be

relatively low. The contrast, moreover, must imitate the consistency of normal feces so it can be retained in the rectum. Consequently, the barium preparation should be a paste, which can be attained with a high concentration of carboxymethyl-cellulose, and be of relatively low radiodensity (60% w/v).

### Evaluating Swallowing Physiology

The MBSS, also known as the videofluoroscopic swallow study (VFSS), is a real-time fluoroscopic radiologic exam used to assess the physiology of swallowing (Figure 3). Its purpose is to obtain a systematic and reproducible assessment of the structure and function of the swallowing mechanism, and determine compensatory strategies for any abnormalities. This is a single-contrast examination, so the  $\text{BaSO}_4$  preparations must contain a low-to-moderate radiodensity (40% w/v). (Table 2) Perhaps more importantly for  $\text{BaSO}_4$  preparations for the MBSS/VFSS, a consistent selection of standardized viscosities must be available. Typical consistencies include thin liquid, nectar, thin honey, honey, puree/pudding, and solid. Moreover, these viscosities must be achieved with non-sticky starches and sugars—no acacia or tragacanth gum, to avoid mucosal coating. Finally, they must be agreeable and food-like, providing adequate “mouthfeel,” or texture, and include sweetness and flavoring for palatability.

Note that carboxymethyl-cellulose is present as a thickener in all liquid  $\text{BaSO}_4$  preparations used for the MBSS. However, the low concentrations found in these liquid preparations are not sufficient to provide  $\text{BaSO}_4$  particles with enough electrostatic attraction to adhere to the inner lining of the GI tract, so there is no coating effect. When carboxymethyl-cellulose is added in a concentration sufficient to create a pudding for MBSS, the electrostatic attraction to the GI inner lining is counteracted by other additives.

Why can’t “regular” GI barium products suitable for single-contrast imaging be used for the MBSS? Because these products lack the precise, standardized viscosities that the MBSS products possess. During development, the viscosity of each MBSS barium product, from thin liquid to pudding, was selected to best reveal physiologic deficiencies in the swallowing mechanism. The use of these products is critical to performing an accurate,



**FIGURE 3.** Representative image from a modified barium swallow study (MBSS) (Image courtesy of: Jo Ann Puntill-Sheltman, SLP, Intermountain St. George Regional Hospital, UT).

reproducible MBSS;<sup>5</sup> they also improve patient safety, increase efficiency, and reduce waste. Simply diluting standard BaSO<sub>4</sub> preparations for the MBSS does not eliminate mucosal coating, creates different (and possibly excessively low) radiodensities, creates unknown viscosities, and dilutes the helpfulness of the additives in unpredictable, and likely unfavorable, ways.

An oft-stated concern with the MBSS is aspiration of BaSO<sub>4</sub> preparations. Per the ACR Manual on Contrast Media,<sup>3</sup> aspirated barium contrast agent is usually mobilized proximally by the ciliary action of normal bronchial epithelium. However, damaged epithelium from bronchial disease delays this process. If not completely expectorated, retained BaSO<sub>4</sub> particles can remain indefinitely and may cause inflammation. As is true for any liquid, high-volume aspiration of barium-containing contrast can lead to acute respiratory distress or pneumonia.<sup>6</sup> To minimize risk, preparations approved for the MBSS have a relatively

low BaSO<sub>4</sub> concentration (40% w/v) and have no sticky gums, both of which assist in clearance. Iodinated contrast media are also not recommended for the MBSS. Ionic high-osmolar contrast media (HOCM), if aspirated, may cause life-threatening pulmonary edema.<sup>3</sup> Nonionic low-osmolar CM (LOCM), while much safer to aspirate by themselves, are all “thin liquids;” therefore, for a full swallowing evaluation, they would have to be mixed with various foods/food additives, whose viscosities are not standardized, and would be nonsterile and possibly dangerous to aspirate.

### Barium Preparations for CT

Three CT applications utilize barium contrast: bowel marking, for standard CT of the abdomen/pelvis; tagging residual solid stool, for CT colonography (CTC; residual liquid stool is tagged with iodinated CM); and bowel distention at near-water density, for CT enterography (CTE).

The function of barium preparations for standard CT of the abdomen/pelvis is to mark bowel loops in order to distinguish them from adjacent structures such as vessels, tumors, and nodes. BaSO<sub>4</sub> preparations for standard CT should: be at 2% w/v concentration, which is sufficient to reveal enhancement; be highly palatable for patient compliance; and contain sorbitol to maintain filling and promote bowel transit.

Barium preparations for CTC are used to tag residual solid stool fragments to distinguish them from polyps. BaSO<sub>4</sub> preparations for this application should: be at 40% w/v concentration; contain carboxymethyl-cellulose (for tagging); be highly palatable; and come packaged and labeled for home use.

Barium-containing contrast for CTE is used to distend bowel loops at near-water density, facilitating the assessment of IV contrast-enhanced bowel wall for involvement with inflammatory bowel disease. For this application, BaSO<sub>4</sub> preparations should: be at no more than

0.1% w/v concentration; include natural gum to provide substance; and contain sorbitol to maintain filling and promote bowel transit.

### Conclusions

Barium sulfate provides barium-containing contrast agents with two specific properties: radiodensity and physical density. Radiodensity, determined by the BaSO<sub>4</sub> concentration, is adjusted for the imaging technology, technique, and structure(s) of interest. All other ingredients provide the other useful properties present in BaSO<sub>4</sub> products: BaSO<sub>4</sub> particle suspension; mucosal coating; viscosity and texture, which are both important for MBSS preparations; sweetness; filling and laxative effect; preservation; foaming prevention; and flavoring. Selecting the right BaSO<sub>4</sub> product for the right exam requires an understanding of the body structures being imaged and the diseases being evaluated. Each imaging technology and clinical application carries not only its own optimal BaSO<sub>4</sub> concentration or concentration range, but also an optimal combination of additives that permit evaluation of the anatomy and/or function of interest.

### References

1. National Center for Biotechnology Information. PubChem Periodic Table of Elements. Barium (Element). Available at: <https://pubchem.ncbi.nlm.nih.gov/element/56>. Accessed February 7, 2021.
2. Miller-Keane Encyclopedia & Dictionary of Medicine, Nursing & Allied Health. Revised Reprint, 7th Edition, Elsevier, Amsterdam.
3. American College of Radiology (ACR) Committee on Drugs and Contrast Media. ACR Manual on Contrast Media, 2020. Available at: [https://www.acr.org/-/media/ACR/files/clinical-resources/contrast\\_media.pdf](https://www.acr.org/-/media/ACR/files/clinical-resources/contrast_media.pdf). Accessed February 7, 2021.
4. Goldner RD, Adams DO. The structure of mononuclear phagocytes differentiating in vivo. III. The effect of particulate foreign substances. *Am J Pathol*. 1977;89:335-350.
5. Hazelwood RJ, Armeson KE, Hill EG, Bonilha HS, Martin-Harris B. Identification of Swallowing Tasks From a Modified Barium Swallow Study That Optimize the Detection of Physiological Impairment. *J Speech Lang Hear Res*. 2017;60:1855-1863.
6. Gelfand DW. Complications of gastrointestinal radiologic procedures: I. Complications of routine fluoroscopic studies. *Gastrointest Radiol*. 1980;5:293-315.

Supported by an educational grant from  
Bracco Diagnostics, Inc.

