Summary Report

Clindamycin hydrochloride

Prepared for:

Food and Drug Administration
Clinical use of bulk drug substances nominated for inclusion on the 503B Bulks List
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Prepared by:

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Frequently Used Abbreviations

API	Active Pharmaceutical Ingredient
EMA	European Medicines Agency
EU	European Union
FDA	Food and Drug Administration
IRB	Institutional Review Board
OTC	Over-the-counter
ROA	Route of administration
SME	Subject matter expert
UK	United Kingdom
US	United States

INTRODUCTION

This report was created to assist the Food and Drug Administration (FDA) in their evaluation of the use of clindamycin hydrochloride (clindamycin HCl; UNII code: 3U02EL437C; T20OQ1YN1W), which was nominated for use as a bulk drug substance in compounding by outsourcing facilities under section 503B of the Federal Food, Drug, and Cosmetic Act.

The aim of this report was to describe how clindamycin HCl is used in clinical research and practice to diagnose, prevent, or treat disease. Due to the broad, exploratory nature of this aim, scoping review methodology was used. Following the scoping review framework, a systematic literature review was conducted and healthcare practitioners were consulted to identify how clindamycin HCl has been used historically and currently.[1-3] Assessment of study quality and risk of bias were not performed because the aim of this report was not to make specific recommendations on the use of this substance in clinical practice.[1,4,5] Rather, the aim was to summarize the available evidence on the use of clindamycin HCl and thereby assist the FDA to determine whether there is a need for the inclusion of this substance on the 503B Bulks List.

REVIEW OF NOMINATION

Clindamycin HCl was nominated for inclusion on the 503B Bulks List by Triangle Compounding Pharmacy, Inc. Clindamycin HCl was nominated for treatment of bacterial infections via a 25-200 mg oral capsule, 25 mg-200 mg/mL oral suspension, and a 1-2.5% topical cream, ointment, gel, or solution.

The nominator provided references from published peer-reviewed literature to describe the pharmacology and support the clinical use of clindamycin HCl.[6-12]

Reasons provided for nomination to the 503B Bulks List included:

- Allergies and intolerance to excipients
- Commercially available capsules/tablets not appropriate for topical preparation
- Need for a higher dose than what is commercially available

METHODOLOGY

Background information

The national medicine registers of 13 countries and regions were searched to establish the availability of clindamycin HCl products in the United States (US) and around the world. The World Health Organization, the European Medicines Agency (EMA), and globalEDGE were used to identify regulatory agencies in non-US countries. The medicine registers of non-US regulatory agencies were selected for inclusion if they met the following criteria: freely accessible; able to search and retrieve results in English language; and desired information, specifically, product trade name, active ingredient, strength, form, route of administration (ROA), and approval status, provided in a useable format. Based on these criteria, the medicine registers of 13 countries/regions were searched: US, Canada, European Union (EU), United Kingdom (UK), Ireland, Belgium, Latvia, Australia, New Zealand, Saudi Arabia, Abu Dhabi, Hong Kong, and Namibia. Both the EMA and the national registers of select EU countries (Ireland, UK, Belgium, and Latvia) were searched because some medicines were authorized for use in the EU and not available in a member country and vice versa.

Each medicine register was searched for clindamycin HCl; name variations of clindamycin HCl were entered if the initial search retrieved no results. The following information from the search results of each register was recorded in a spreadsheet: product trade name; active ingredient; strength; form; ROA; status

and/or schedule; approval date. Information was recorded only for products with strengths, forms, and/or ROA similar to those requested in the nominations.

In addition to the aforementioned medicine registers, the DrugBank database (version 5.1.5) and the Natural Medicines database were searched for availability of over-the-counter (OTC) products containing clindamycin HCl. The availability of OTC products (yes/no) in the US and the ROA of these products were recorded in a spreadsheet. Individual product information was not recorded.

Systematic literature review

Clindamycin HCl is a component of an FDA-approved product that was discontinued by the manufacturer, not for safety or efficacy reasons. The nominated compounded products did not differ substantially from the commercially available product. Therefore, a systematic literature review was not conducted.

Interviews

Semi-structured interviews with subject matter experts (SMEs) were conducted to understand how and in what circumstances clindamycin HCl was used in a clinical setting. Using the indication from the nomination the following medical specialties that would potentially use clindamycin HCl were identified: dermatology, infectious disease, and primary care and internal medicine. Potential SMEs within the relevant medical specialties were identified through recommendations and referrals from professional associations, colleagues' professional networks, and authors of relevant literature. In addition, the American Society of Health-System Pharmacists (ASHP) and select outsourcing facilities were contacted for interviews and referrals to additional SMEs. SMEs provided oral informed consent to be interviewed and audio recorded. Interviews lasting up to 60 minutes were conducted via telephone, audio recorded, and professionally transcribed. The transcriptions and notes were entered into NVivo 12 (QSR International) for qualitative data analysis. Several members of the research team independently coded the transcriptions of two representative interviews for themes. The team members discussed the codes that emerged from their independent analysis, as well as those codes that were determined a priori. The code book was developed out of the integration of these coding schemes.

Survey

A survey was distributed to the members of professional medical associations to determine the use of clindamycin HCl in clinical practice. The online survey was created using Qualtrics® software (refer to Appendix 2 for complete survey). A Google™ search was conducted to identify the professional associations in the US for the relevant medical specialties. An association's website was searched to identify the email of the executive director, regulatory director, media director, association president, board members, or other key leaders within the organization to discuss survey participation. If no contact information was available, the "contact us" tab on the association website was used. An email describing the project and requesting distribution of the survey to the association's members was sent to the identified person(s). Associations that declined, did not respond, or did not provide significant data in project Year 1, were not contacted to distribute the project Year 2 surveys.

The survey was posted on the project website and the survey link was distributed to the associations that agreed to participate (refer to Appendix 3 for associations that participated and those that did not).

Participation was anonymous and voluntary. The estimated time for completion was 15 minutes with a target of 50 responses per survey. The University of Maryland, Baltimore Institutional Review Board (IRB) and the FDA IRB reviewed the interview and survey methods and found both to be exempt. The Office of Management and Budget approved this project.

CURRENT AND HISTORIC USE

Results of background information

- Clindamycin HCl is available as an FDA-approved oral capsule. The other nominated dosage forms are not available as the HCl salt but are available as other salt forms.
- Clindamycin HCl is not available as an OTC product in the US.
- There is a current United States Pharmacopeia (USP) monograph for clindamycin HCl.
- Clindamycin HCl is available in the nominated dosage form and ROA in Abu Dhabi, Australia, Canada, Hong Kong, Ireland, Latvia, Namibia, New Zealand, Saudi Arabia, and UK.

Table 1. Currently approved products – US[a]

Active Ingredient	Concentration	Dosage Form	Route of Administration	Status	Approval Date[b]
Clindamycin HCl	EQ 75-300 mg base	Capsule	Oral	Prescription	Approved Prior to Jan 1, 1982

Abbreviations: "–", not mentioned; EQ, equivalent to

[a]Source: US FDA *Approved Drug Products with Therapeutic Equivalence Evaluations* (Orange Book).

[b]If multiple approval dates and/or multiple strengths, then earliest date provided.

Table 2. Currently approved products – select non-US countries and regions[a]

Active Ingredient	Concentration	Dosage Form	Route of Administration	Approved for Use		
				Country	Status	Approval Date[b]
Clindamycin HCl	150 mg, 300 mg	Capsule	Not mentioned	Abu Dhabi	Active	–
	150 mg, 500 mg			Namibia	–	7/8/1970
	150 mg			New Zealand	Prescription	8/24/1972
	150 mg		Oral	Australia	Prescription	8/2/1991
	150 mg, 300 mg			Canada	Prescription	12/31/1970
	150 mg			Hong Kong	Prescription	12/8/2015
	300 mg			Ireland	Prescription, non-renewable	5/15/2009
Clindamycin	150 mg, 300 mg			Latvia	Prescription	7/21/1998
Clindamycin HCl	150 mg, 300 mg			Saudi Arabia	Prescription	–
	75 mg, 150 mg 300 mg			UK	Prescription	2/20/1989
	10 mg/mL	Solution	Not mentioned	Namibia	–	4/14/1983
	1%		Topical	Australia	Prescription	11/23/1998
Clindamycin	20 mg/g	Cream	Vaginal	Latvia	Prescription	10/14/1998

Abbreviations: "– ", not mentioned.

[a]Medicine registers of national regulatory agencies were searched if they met the following criteria: freely accessible; able to search and retrieve results in English language; and desired information (product trade name, active ingredient, strength, form, ROA, and approval status) provided in a useable format. Information was recorded only for products with strengths, forms, and/or ROA similar to those requested in the nominations. See Methodology for full explanation.

[b]If multiple approval dates and/or multiple strengths, then earliest date provided.

Results of literature review

No literature review was conducted.

Pharmacology and historical use

Two studies were identified that did not meet the inclusion criteria but provided valuable information about the pharmacology and historical use of clindamycin HCl.

Clindamycin has a repulsive odor and taste which makes it less favorable for pediatric patients since they are "more sensitive to bitter tasting substances than adults".[13] It is available as an oral solution in the palmitate salt form, which was "synthesized to reduce the bitterness of clindamycin," but this did not solve the problem completely.[13] Alayoubi et al successfully formulated an oral suspension of clindamycin HCl that masked the taste.[13]

In 1979, a double-blind study was conducted comparing 1% topical solutions of clindamycin phosphate and clindamycin HCl for the treatment of acne.[14] The solutions were randomly applied on opposite sides of the face.[14] Twenty-one patients were enrolled; only 15 received treatment for at least 3 months.[14] Out of these 15 patients, "4 responded better to topical clindamycin phosphate, 4 responded better to the HCl form, and 7 responded equally to both solutions," leading to the conclusion that both forms seemed to be equivalent.[14]

Table 3. Types of studies

No literature review was conducted

Table 4. Number of studies by country

No literature review was conducted

Table 5. Summary of included studies

No literature review was conducted

Table 6. Dosage by indication – US

No literature review was conducted

Table 7. Dosage by indication – non-US countries

No literature review was conducted

Table 8. Number of studies by combinations

No literature review was conducted

Table 9. Compounded products – US

No literature review was conducted

Table 10. Compounded products – non-US countries

No literature review was conducted

Results of interviews

Two hundred eighty-five SMEs were contacted for interviews; 96 agreed to be interviewed, and 189 declined or failed to respond to the interview request. Five SMEs discussed clindamycin HCl. Amongst these 5 SMEs, there were 4 medical doctors and 1 pharmacist. The SMEs specialized and/or were board-certified in dermatology, infectious disease, primary care and family medicine, working in consulting and academic medical practice. The SMEs had been in practice for 9 to 40 years.

Clindamycin is commercially available in various topical dosage forms as the phosphate salt and is commonly used for treatment of dermatologic conditions, specifically acne. Acne requires repeated treatments so oral products are not generally due to gastrointestinal concerns. While there are some bacteria associated with acne, acne per se is not thought of as a bacterial infection. It is thought that the anti-inflammatory property of clindamycin is the reason why it works on acne. Additionally, there are concerns with antibiotic resistance associated with long-term use; the American Academy of Dermatology has released recommendations against the use of continuous long-term antibiotics. For other cutaneous infections, like impetigo, erysipelas, or cellulitis, one SME stated it is better to use an approved systemic antibiotic as compared to an experimental modality. Clindamycin is also used as an irrigation solution for surgical procedures.

The need for a compounded clindamycin preparation may be the result of practitioners having a preferred multi-ingredient combination, like with a retinoid or benzoyl peroxide for treatment of acne, or the need for the addition of an anti-inflammatory agent or something to increase penetration and effectiveness. While clindamycin is relatively safe and there is likely minimal harm in compounding clindamycin HCl as a topical product, there are concerns about the stability of the compounded preparation due to the drug not staying active for long and inappropriate use leading to multi-drug resistance. Additionally, with the availability of other options, like clindamycin phosphate, which is known to be stable, there is not necessarily a need for a compounded version for office use.

Some SMEs had experience using compounded products in general, but none are currently using compounded clindamycin HCl. Additionally, the SMEs did not identify a need for using the hydrochloride salt over the phosphate salt.

Results of survey

Eight people responded to the survey; refer to Table 11 for respondent characteristics.

Among respondents, 8 (100%) used clindamycin HCl. Respondents used clindamycin HCl as a topical cream (5, 63% of respondents), topical gel (4, 50%), topical ointment (3, 38%), and a topical solution (3, 38%). Respondents used clindamycin HCl for treatment of bacterial infections (5, 63%) and acne (2, 25%) (refer to Table 12).

Survey respondents utilized compounded clindamycin HCl due to a lack of commercial products in an appropriate dosage form, strength, or combination (4, 50% of respondents) and patient allergies (2, 25%).

One (13%) respondent used compounded clindamycin HCl because "customized RX options from an FDA Registered 503B are superior with my patient outcomes" and 1 (13%) responded that the "generic is just as effective." Refer to Table 13 for reasons for using compounded clindamycin HCl. Explanation for using compounded clindamycin HCl due to patient allergies included "commercially available drug formulas have known harmful allergens or irritants. My compounded medications are free from irritants and other potential harmful ingredients."

The majority of respondents (5, 63%) did stock non-patient-specific compounded clindamycin HCl at their practice. Respondents that did stock non-patient-specific clindamycin HCl compounded the product at their practice (20% of respondents) or purchased, or had the patient purchase, the product from an outsourcing facility (80%). Refer to Table 14 for how respondents obtained compounded clindamycin HCl.

Table 11. Characteristics of survey respondents

Terminal Clinical Degree	**Responses, n (N=8)**
Doctor of Medicine (MD)	5
Doctor of Osteopathic Medicine (DO)	1
Nurse Practitioner (NP)	1
No Response	1
Practice Setting	**Response, n (N=8)**
Physician office or private practice	7
No response	1

Table 12. Conditions for which clindamycin HCl prescribed or administered

Condition	**Responses, n (N=8)[a]**
Bacterial infections	5
Acne	2
No Response	2

[a]Survey respondents allowed to select multiple conditions.

Table 13. Reasons for using compounded clindamycin HCl

Reason	Responses, n (N=8)[a]
Commercial product not available in desired dosage form, strength, or combination	4
Patient allergies prevent use of commercial products	2
Generic is just as effective	1
Commercially available drugs have harmful allergens or irritants	1
No response	2

[a]Survey respondents allowed to select multiple reasons.

Table 14. Use of non-patient-specific compounded clindamycin HCl

Do you stock non-patient-specific compounded clindamycin HCl at your practice?	**Responses, n (N=8)**
Yes	5
No	1
No response	2
How do you obtain your stock of non-patient-specific compounded clindamycin HCl?	
Compound yourself at practice	1
Product compounded by in-house pharmacy	0
Purchase from compounding pharmacy	0
Purchase from outsourcing facility	4

CONCLUSION

Clindamycin HCl was nominated for inclusion on the 503B Bulks List as an oral capsule or suspension, and a topical cream, gel, ointment, and solution to treat bacterial infections. Clindamycin HCl is available in the nominated dosage form and ROA in Abu Dhabi, Australia, Canada, Hong Kong, Ireland, Latvia, Namibia, New Zealand, Saudi Arabia, and UK.

From the interviews conducted, topical clindamycin is used primarily for acne. Background literature indicated that the repulsive odor and taste of clindamycin drives the need for alternative oral formulations to improve adherence in children. The interviewed SMEs did not identify a need for using the HCl salt over the phosphate salt. There was a concern for antibiotic resistance with long-term use.

From the survey responses, 8 out of 8 respondents used clindamycin HCl. The most common indication respondents used compounded clindamycin HCl for was bacterial infections. A lack of commercially available products in the desired dosage form, strength, or combination and patient allergies to the commercially available products were some of the reasons for using the compounded clindamycin HCl product over an FDA-approved product. Five respondents reported stocking compounded clindamycin HCl at their practice setting.

REFERENCES

1. Arksey H, O'Malley L. Scoping studies: Towards a methodological framework. *International Journal of Social Research Methodology: Theory and Practice.* 2005;8(1):19-32.
2. Colquhoun HL, Levac D, O'Brien KK, et al. Scoping reviews: time for clarity in definition, methods, and reporting. *J Clin Epidemiol.* 2014;67(12):1291-1294.
3. Levac D, Colquhoun H, O'Brien KK. Scoping studies: Advancing the methodology. *Implementation Science.* 2010;5(1).
4. Peters MDJ, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. *International Journal of Evidence-Based Healthcare.* 2015;13(3):141-146.
5. Munn Z, Peters MDJ, Stern C, Tufanaru C, McArthur A, Aromataris E. Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. *BMC Med Res Methodol.* 2018;18(1):143-143.
6. Daum RS, Miller LG, Immergluck L, et al. A placebo-controlled trial of antibiotics for smaller skin abscesses. *N Engl J Med.* 2017;376(26):2545-2555.
7. Leijtens B, Elbers JBW, Sturm PD, Kullberg BJ, Schreurs BW. Clindamycin-rifampin combination therapy for staphylococcal periprosthetic joint infections: A retrospective observational study. *BMC Infect Dis.* 2017;17(1):321-321.
8. Ortega E, Gutiérrez L, Bernad MJ, Salmerón F, Juárez I, Vargas D. Evaluation of different oral formulations of clindamycin extended release in dogs. *Drug Res (Stuttg).* 2017;67(1):32-37.
9. Tariq N, Basharat A, Khan DH, Fahim A, Khan MH. Treatment for symptomatic bacterial vaginosis: a randomized controlled trial. *J Coll Physicians Surg Pak.* 2017;27(11):686-689.
10. Wargo KA, McCreary EK, English TM. Vancomycin combined with clindamycin for the treatment of acute bacterial skin and skin-structure infections. *Clin Infect Dis.* 2015;61(7):1148-1154.
11. Zarandi ER, Mansouri S, Nakhaee N, Sarafzadeh F, Moradi M. Toxin production of clostridium difficile in sub-mic of vancomycin and clindamycin alone and in combination with ceftazidime. *Microb Pathog.* 2017;107:249-253.
12. Zarandi ER, Mansouri S, Nakhaee N, Sarafzadeh F, Moradi M. Effect of sub-mic of vancomycin and clindamycin alone and in combination with ceftazidime on clostridium difficile surface layer protein a (slpa) gene expression. *Microb Pathog.* 2017;111:163-167.
13. Alayoubi A, Daihom B, Adhikari H, Mishra S, Helms R, Almoazen H. Development of a taste-masked oral suspension of clindamycin HCl using ion exchange resin Amberlite IRP 69 for use in pediatrics. *Drug Development and Industrial Pharmacy.* 2016;42(10):1579-1589.
14. Guin JD. Topical clindamycin: A double-blind study comparing clindamycin phosphate with clindamycin hydrochloride. *International Journal of Dermatology.* 1979;18(2):164-166.

APPENDICES

Appendix 1. Search strategies for bibliographic databases

No literature review was conducted

Appendix 2. Survey instrument

Welcome. We want to understand your clinical use of compounded clindamycin hydrochloride. Your feedback will help the Food and Drug Administration (FDA) develop a list of drugs that can be used in compounding by 503B outsourcing facilities. Your anonymous responses will be shared with the FDA. The time required to complete this survey is approximately 10-15 minutes.

If you have additional questions or concerns about this study, please email: compounding@rx.umaryland.edu. If you have questions about your rights as a research subject, please contact HRPO at 410-760-5037 or hrpo@umaryland.edu.

Thank you,
Dr. Ashlee Mattingly, Principal Investigator
The University of Maryland School of Pharmacy

An agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number.

OMB Control No. 0910-0871
Expiration date: June 30, 2022

1. How familiar are you with the following terms?

	Very familiar	Somewhat familiar	Not familiar
Compounded drugs (medications prepared to meet a patient-specific need)	o	o	o
503A Compounding pharmacy (a pharmacy that prepares compounded medications prescribed by practitioners to meet a patient-specific need)	o	o	o
503B Outsourcing facility (a facility that compounds larger quantities without the receipt of a patient-specific prescription)	o	o	o

2. Do you prescribe or administer clindamycin hydrochloride to your patients?

   o Yes
   o No

3. Do you prescribe or administer clindamycin hydrochloride by any of the following dosage forms and/or routes of administration? (check all that apply)

   - o Oral suspension
   - o Topical cream
   - o Topical gel
   - o Topical ointment
   - o Topical solution
   - o None of the above

4. I prescribe or administer clindamycin hydrochloride for the following conditions or diseases: (check all that apply)

   - o Bacterial infections
   - o Other (please explain) _____

5. I use compounded clindamycin hydrochloride because: (check all that apply)

   - o Commercial products are not available in the dosage form, strength, or combination I need. (please explain) _____
   - o Patient allergies prevent me from using commercially available products. (please explain) _____
   - o Patient conditions prevent me from using commercially available products. (please explain) _____
   - o There are no commercially available products containing clindamycin hydrochloride.
   - o Other (please explain) _____

6. Do you stock non-patient-specific compounded clindamycin hydrochloride at your practice?

   - o Yes
   - o No
   - o I'm not sure

7. I obtain compounded clindamycin hydrochloride from the following: (check all that apply)

   - o Compound myself at my practice
   - o Have the product compounded by an in-house pharmacy
   - o Purchase, or have a patient purchase, from a compounding pharmacy
   - o Purchase, or have a patient purchase, from an outsourcing facility
   - o Other (please explain) _____

8. What is your practice setting? (check all that apply)

- o Physician office/private practice
- o Outpatient clinic
- o Hospital/health system
- o Academic medical center
- o Emergency room
- o Operating room
- o Other (please describe) _____

9. What degree do you hold? (check all that apply)

- o Doctor of Medicine (MD)
- o Doctor of Osteopathic Medicine (DO)
- o Doctor of Medicine in Dentistry (DMD/DDS)
- o Doctor of Pharmacy (PharmD) or Bachelor of Science in Pharmacy (BS Pharm)
- o Naturopathic Doctor (ND)
- o Nurse Practitioner (NP)
- o Physician Assistant (PA)
- o Other (please describe) _____

Appendix 3. Survey distribution to professional associations

Specialty	Association[a]	Agreed/Declined, Reason for Declining
Allergy/Immunology	American Academy of Allergy, Asthma, and Immunology (AAAI)	Declined – survey not approved
Anesthesia	American Society of Regional Anesthesia and Pain Medicine (ASRA)	Declined – failed to respond
	Society for Ambulatory Anesthesia (SAMBA)	Declined – failed to respond
	Society for Neuroscience in Anesthesiology and Critical Care	Declined – failed to respond
Critical Care	Critical Care Societies Collaborative	Declined – failed to respond
Dentistry & Oral Medicine	Academy of General Dentistry (AGD)	Declined – provided interview referrals
	American Dental Association (ADA)	Declined – failed to respond
Dermatology	American Academy of Dermatology (AAD)	Agreed
	American Osteopathic College of Dermatology (AOCD)	Declined – not interested
Endocrinology	The Endocrine Society (ENDO)	Agreed
	Pediatric Endocrine Society	Agreed
Gastroenterology	American Gastroenterological Association (AGA)	Declined – failed to respond
	Obesity Medicine Association (OMA)	Declined – did not have anyone to contribute to research
Hematology	American Society of Hematology (ASH)	Declined – does not distribute surveys
Infectious Disease	American Academy of HIV Medicine (AAHIVM)	Declined – failed to respond
Medicine	American Medical Association (AMA)	Declined – failed to respond

Naturopathy	American Association of Naturopathic Physicians (AANP)	Agreed
	The Oncology Association of Naturopathic Physicians (OncANP)	Agreed
Nephrology	American College of Clinical Pharmacists: Nephrology Practice Network	Agreed
	American Society of Nephrology	Declined – provided interview referrals
Nutrition	American Society for Parenteral and Enteral Nutrition (ASPEN)	Declined – provided interview referrals
Obstetrics and Gynecology	American Gynecological and Obstetrical Society (AGOS)	Declined – failed to respond
	Nurse Practitioners in Women's Health	Agreed
Ophthalmology	American Academy of Ophthalmology (AAO)	Agreed
Otolaryngology	American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS)	Declined – survey not approved
Pain Management	American Academy of Pain Medicine (AAPM)	Declined – survey not approved
	American Academy of Physical Medicine and Rehabilitation	Declined – failed to respond
Pediatrics and Neonatology	American Academy of Pediatrics (AAP)	Agreed
Primary Care	American College of Physicians (ACP)	Declined – failed to respond
Psychiatry	American Academy of Clinical Psychiatrists	Declined – failed to respond
	American Association for Geriatric Psychiatry	Declined – failed to respond
Rheumatology	American College of Rheumatology (ACR)	Agreed

Surgery	Ambulatory Surgery Center Association (ASCA)	Agreed
	American Academy of Orthopaedic Surgeons (AAOS)	Declined – no interest in participation from members
	American Association of Hip and Knee Surgeons (AAHKS)	Declined – only send surveys from members
	American College of Surgeons (ACS)	Agreed
	American Society for Metabolic and Bariatric Surgery (AMBS)	Declined – only send surveys from members
	The Association of Bone and Joint Surgeons	Declined – failed to respond
	Physician Assistants in Orthopaedic Surgery	Declined – failed to respond
	Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)	Declined – failed to respond
	Society of Gynecologic Surgeons (SGS)	Declined – policy limits number of surveys per year and do not have a method to identify if any of the SGS members are using ipamorelin
Toxicology	American Academy of Environmental Medicine (AAEM)	Declined – failed to respond
Urology	Sexual Medicine Society of North America (SMSNA)	Agreed

[a]Associations that declined in Year 1 were not contacted in Year 2.