Summary Report

Haloperidol

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

ABH	Lorazepam, diphenhydramine, and haloperidol
ABHR	Lorazepam, diphenhydramine, haloperidol, and metoclopramide
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 haloperidol (UNII code: J6292F8L3D), 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 haloperidol 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 haloperidol 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 haloperidol 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

Haloperidol was nominated for inclusion on the 503B Bulks List by Triangle Compounding Pharmacy, Inc. Haloperidol was nominated for schizophrenia, psychoses, schizoaffective disorder, delusional disorders, Tourette syndrome, agitation, and restlessness via rectal suppositories and topical dosage forms. The nominator stated that strengths to be compounded vary, with previous doses ranging from 0.5 mg to 2 mg.

The nominator did not provide references from published peer-reviewed literature to describe the pharmacology and support the clinical use of haloperidol.

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

- Haloperidol can be used topically for hospice patients who may not be able to take drugs orally.
- A concentration greater than what is available commercially is needed to allow for a decreased volume to be topically applied to a small area.
- The consistency of the topical product could be adversely affected by the aqueous formulations of the commercially available product.
- The commercially available products may contain inappropriate excipients for compounding.
- If a commercial product becomes unavailable, the bulk product can be used to compound a product to bridge the gap.

METHODOLOGY

Background information

The national medicine registers of 13 countries and regions were searched to establish the availability of haloperidol 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 haloperidol; name variations of haloperidol 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 haloperidol. 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

Search strategy

A medical librarian constructed comprehensive search strategies for Ovid MEDLINE and Embase. The search strategies used a combination of controlled vocabulary terms and keywords to describe two concepts: haloperidol, and topical or rectal administration or form (refer to Appendix 1 for full search strategies). Keywords for brand or proprietary products were not included in the search strategy because studies that utilized such products were excluded. Results were limited human studies in English language. Searches were conducted on March 24, 2020. The reference lists of relevant systematic reviews and meta-analyses were reviewed to identify additional studies. In addition, the ECRI Guidelines Trust® repository was searched on March 24, 2020 for clinical practice guidelines that recommended the use of haloperidol and provided sufficient information on dosing and administration.

Results were exported to EndNote for Windows version X9.2 (Clarivate Analytics), and duplicates were removed. The de-duplicated results were uploaded to Covidence (Veritas Health Innovation) for screening.

Study selection

Studies in which haloperidol was used in the nominated dosage form, ROA, and/or combination product to diagnose, prevent or treat the nominated disease or condition, or other conditions not specified in the nomination, were included. Studies were excluded if they were: written in a language other than English; reviews or meta-analyses; surveys or questionnaires (cross-sectional design); designed to evaluate cost-effectiveness, mechanism of action, pre-clinical use, safety, or toxicity; or any study design other than a randomized controlled trial conducted in a non-US country. Studies were also excluded if haloperidol was used as: a brand or proprietary product; an FDA-approved product in the nominated dosage form, ROA, or combination; or a dosage form, ROA, or combination that was not nominated. Studies in which haloperidol was used to diagnose, prevent, or treat autism were excluded due to a separate project examining the use of compounded substances in individuals with autism. Studies that did not meet the inclusion criteria, but provided valuable information about the pharmacological or current or historical use of the substance were noted and put in a separate group in the EndNote library. Two reviewers independently screened titles and abstracts, and reviewed full-text articles. A third reviewer reconciled all disagreements.

Data extraction

The following information was recorded in a standard data extraction form: author names; article title; journal; year of publication; country; study type; historical use of haloperidol; setting; total number of patients; number of patients who received haloperidol; patient population; indication for use of haloperidol; dosage form and strength; dose; ROA; frequency and duration of therapy; use of haloperidol in a combination product; use and formulation of haloperidol in a compounded product; use of haloperidol compared to FDA-approved drugs or other treatments; outcome measures; authors' conclusions. One reviewer extracted data from the included studies; a second reviewer checked the data extraction.

Interviews

Semi-structured interviews with subject matter experts (SMEs) were conducted to understand how and in what circumstances haloperidol was used in a clinical setting. The systematic literature review and indications from the nomination were reviewed to identify the following medical specialties that would potentially use haloperidol: palliative care, primary care and internal medicine, and psychiatry. 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 haloperidol 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

- Haloperidol is not available as an FDA-approved product in the nominated dosage form and ROA.
- Haloperidol is not available as an OTC product in the US.
- There is a current United States Pharmacopeia (USP) monograph for haloperidol.
- Haloperidol is not available in the nominated dosage form and ROA in any of the foreign medicinal registries searched.

Table 1. Currently approved products – US

No approved products in the US

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

No approved products in the selected non-US countries and regions

Results of literature review

Study selection

Database searches yielded 330 references; 2 additional references were identified from searching ECRI Guidelines Trust® and the references of relevant systematic reviews. After duplicates were removed, 247 titles and abstracts were screened. After screening, the full text of 28 articles was reviewed. Finally, 1 study was included. Twenty-seven studies were excluded for the following reasons: haloperidol only mentioned briefly (9 studies); wrong dosage form or ROA (9); wrong study design (6); haloperidol not used clinically (2); language other than English (1).

Refer to Figure 1 for the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

Characteristics of included studies

There was 1 included descriptive study from the US published in 1998.

A total of 20 patients participated in the study and the primary outcome measured was the symptom of seeing and feeling parasites.

Refer to Table 5 for summary of study country, design, patient population, intervention and comparator, and outcome measures.

Use of haloperidol

Three patients received haloperidol as treatment for psychogenic parasitosis. Two cases used haloperidol intramuscularly and 1 case used haloperidol via an unspecified ROA. The dose, dosage form, and duration of treatment were not specified.

Refer to Table 6 for the summary of dosage by indication.

Haloperidol was not used as a compounded product.

For the included study, the authors' concluding statement did not address the use of haloperidol.[6] Refer to Table 5 for summary of authors' conclusion.

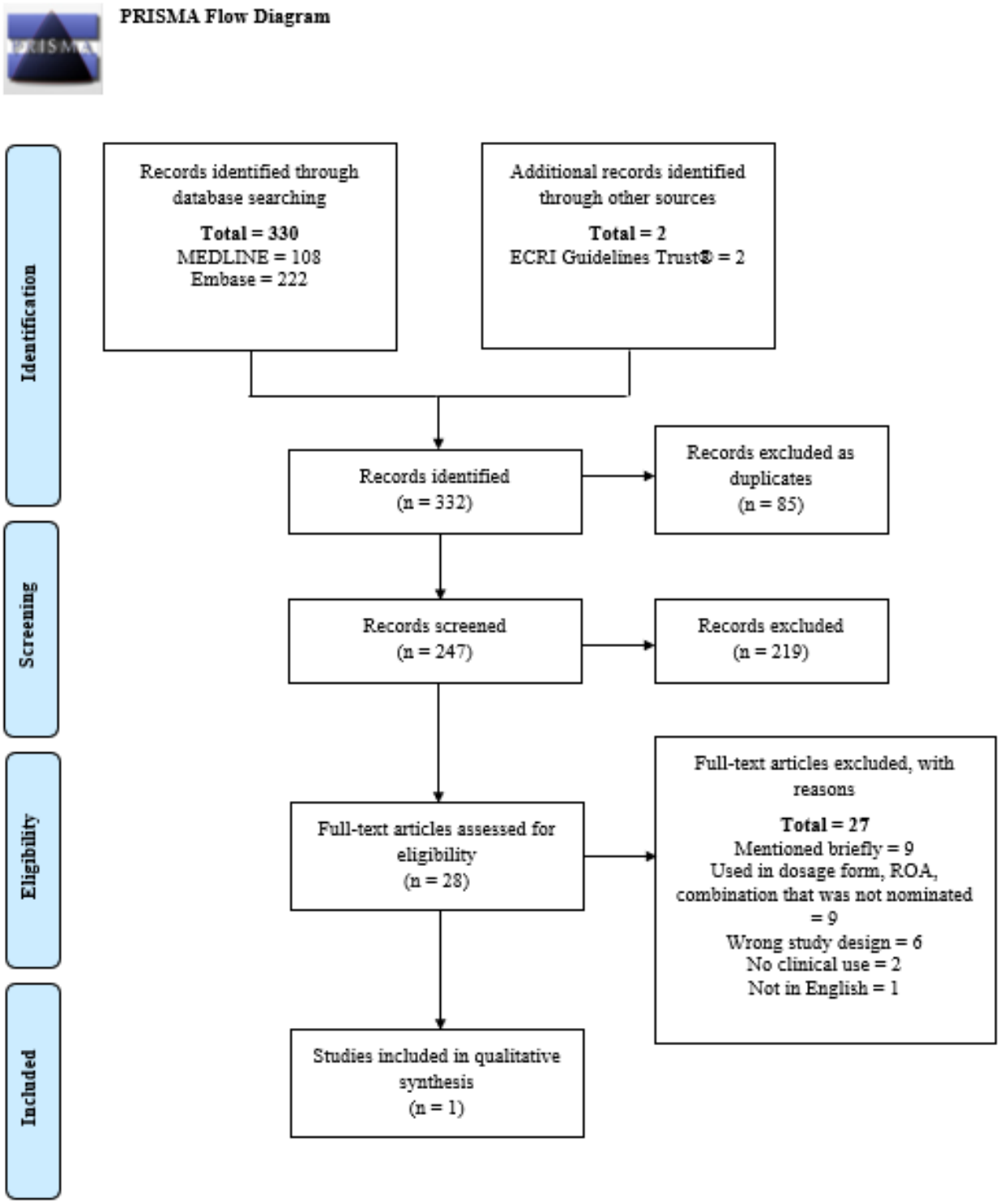
Pharmacology and historical use

In addition to the 1 included study, 3 studies were identified that did not meet the inclusion criteria but provided valuable information about the pharmacology and historical use of haloperidol.

In the American Psychiatric Association practice guideline for use of antipsychotics to treat agitation or psychosis in dementia patients, haloperidol is mentioned briefly.[7] The guideline stated that "In the absence of delirium [and] when nonemergency antipsychotic medication is indicated, haloperidol should not be used as a first-line agent."[7] The guidelines did not specify the dosage form and/or ROA for haloperidol.[7]

There were no studies found that specified the use of haloperidol as a rectal suppository. As for topical haloperidol, one study reported the tolerability of the compounded combination lorazepam, diphenhydramine, haloperidol, and metoclopramide (ABHR) for nausea and vomiting in hospice patients.[8] Haloperidol was used in this combination due to its potent dopamine antagonist properties.[8] The ABHR combination products came in a variety of dosage forms, including suppository, capsule, suspension, troche, and topical gel.[8] The most common ABHR combination dispensed was the topical gel.[8] The authors concluded that the use of ABHR combination was generally well tolerated in most hospice patients.[8] In 2012, the American Academy of Hospice and Palliative Medicine as part of their Choosing Wisely® campaign, recommended that topical lorazepam, diphenhydramine, and haloperidol (ABH) gel not be used for nausea because there have not been any large, well-designed or placebo-controlled studies that have proven the ABH gel to be effective.[9,10] They also stated that "the active ingredients in ABH are not absorbed to systemic levels that could be effective."[9,10]

Figure 1. PRISMA flow diagram showing literature screening and selection.



Adapted from:
Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol.* 2009;62(10):1006-1012. Available from: http://www.prisma-statement.org/.

Table 3. Types of studies

Types of Studies	**Number of Studies**
Descriptive[6]	1
Experimental	0
Observational	0

Table 4. Number of studies by country

Country	**Number of Studies**
US[6]	1
	Total US: 1 Total Non-US Countries: 0

Table 5. Summary of included studies

Author, Year, Country	Study Type[a]	Patient Population (% male, age range)	Intervention/Comparator (# of patients)	Primary Outcome Measure	Authors' Conclusions
Zanol *et al.*, 1998, US[6]	Cases	20 Patients with psychogenic parasitosis (45%, 24-80 y)	Each patient received psychiatric drugs such as pimozide, haloperidol*, methylphenidate, perphenazine, lorazepam, clonazepam, sertraline, paroxetine, fluoxetine. *2 cases used haloperidol intramuscularly, 1 case used haloperidol via an unspecified route of administration	Symptoms of seeing and feeling the parasites	For patients with psychogenic parasitosis, dermatologist and psychiatrists can work together to develop treatment plans to minimize risk and maximize therapy.

[a]As defined by authors.

Table 6. Dosage by indication – US

Indication	Dose	Concentration	Dosage Form	Route of Administration	Duration of Treatment
Psychogenic parasitosis	–	–	–	–	–
	–	–	–	Intramuscular	–

Abbreviation: "–", not mentioned.

Table 7. Dosage by indication – non-US countries

No studies identified from non-US countries

Table 8. Number of studies by combination

No combination products were nominated

Table 9. Compounded products – US

No compounded products from reported studies

Table 10. Compounded products – non-US countries

No compounded products from reported studies

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. Nine SMEs discussed haloperidol. Amongst these 9 SMEs, there were 5 medical doctors, 3 pharmacists, and 1 nurse practitioner. The SMEs specialized and/or were board-certified in child and adolescent psychiatry, geriatrics, internal medicine, oncology/hematology, palliative care, pharmacotherapy, psychiatry, and primary care/family practice, working in academia and academic medical centers. The SMEs had been in practice for 6 to 34 years.

Haldol® (haloperidol) is predominately used for agitation. One SME commented that "back in the day" haloperidol was referred to as "vitamin H" because everyone in nursing homes with agitation would get haloperidol. This SME also stated that "[haloperidol is] just a horrible snow job" and does not serve a useful purpose other than to make the nurses feel better. On the other hand, a different SME said they try haloperidol first in patients with agitated delirium. Other indications mentioned include schizophrenia, extrapyramidal side effects in children, advanced Alzheimer's disease, and Tourette syndrome in children. When treating schizophrenia with haloperidol, there is a risk of involuntary movements. Because of this, one SME was reluctant to use haloperidol in children and adolescents, who are at a greater risk for this side effect. Another SME commented that if a patient needs an antipsychotic, then haloperidol is not a great choice and instead they would use an atypical antipsychotic.

Several SMEs had used haloperidol orally and as an injection. None of the SMEs had used a topical haloperidol formulation, and several expressed that topical haloperidol would have absorption issues. On the contrary, one SME mentioned that the topical formulation would be good to have as an alternative to giving injections to an uncooperative patient. As for the nominated rectal suppository, several SMEs stated they would consider using it. However, one SME commented that they would first use haloperidol intensol, a high concentrated oral solution, before considering the rectal formulation. Another SME stated that haloperidol suppositories have been used before and they would want to have that stocked. One SME stated that there is a huge need for haloperidol in palliative care and hospice so both the topical and rectal formulations would be appropriate. Several SMEs specializing in psychiatry stated that rectal formulations are not used in psychiatry facilities anymore while another commented "in psychiatry, I can't imagine a reason for giving rectal medications."

Results of survey

Zero people responded to the survey distributed via professional medical associations and available on the project website.

Table 11. Characteristics of survey respondents

No respondents to survey distributed via professional medical associations

Table 12. Conditions for which haloperidol prescribed or administered

No respondents to survey distributed via professional medical associations

Table 13. Reasons for using compounded haloperidol

No respondents to survey distributed via professional medical associations

Table 14. Use of non-patient-specific compounded haloperidol

No respondents to survey distributed via professional medical associations

CONCLUSION

Haloperidol was nominated for inclusion on the 503B Bulks List for schizophrenia, psychoses, schizoaffective disorder, delusional disorders, Tourette syndrome, agitation, and restlessness via rectal suppositories and topical dosage forms. Haloperidol is not available in the nominated dosage forms and ROA in the US or in any of the national medical registries searched.

From the literature review and interviews conducted, haloperidol is used to treat agitation. Other indications mentioned include schizophrenia, extrapyramidal side effects in children, advanced Alzheimer's, and Tourette syndrome in children. The literature review found no studies that specified the use of haloperidol as a rectal suppository while 1 study reported the use of haloperidol topically in a compounded combination called ABHR for nausea and vomiting in hospice patients. However, the American Academy of Hospice and Palliative medicine recommended that topical ABH not be used for nausea because its efficacy has not been proven in any large, well-designed or placebo-controlled studies and the active ingredients are not absorbed to systemically effective levels. From the interviews, one SME stated that there is a huge need for haloperidol in palliative care and hospice so both the topical and rectal formulations would be appropriate. None of the SMEs had used a topical haloperidol formulation. Several expressed concerns that topical haloperidol would have absorption issues, while another SME thought this would be good to have as an alternative to giving injections to an uncooperative patient. As a rectal suppository, one SME stated that suppositories have been used before and several SMEs would consider using it. However, a few SMEs specializing in psychiatry stated that rectal formulations are not used in psychiatry facilities anymore.

Zero people responded to the survey distributed via professional medical associations and available on the project website.

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. Zanol K, Slaughter J, Hall R. An approach to the treatment of psychogenic parasitosis. *International Journal of Dermatology.* 1998;37(1):56-63.
7. Reus VI, Fochtmann LJ, Eyler AE, et al. The American Psychiatric Association Practice Guideline on the Use of Antipsychotics to Treat Agitation or Psychosis in Patients With Dementia. *Am J Psychiatry.* 2016;173(5):543-546.
8. Weschules DJ. Tolerability of the compound ABHR in hospice patients. *J Palliat Med.* 2005;8(6):1135-1143.
9. Choosing Wisely: Five Things Physicians and Patients Should Question in Hospice and Palliative Medicine. American Academy of Hospice and Palliative Medicine. http://aahpm.org/outreach/choosing-wisely. Accessed December 8, 2020.
10. American Academy of Hospice and Palliative Medicine Recommendations. American Board of Internal Medicine. Choosing Wisely Web site. https://www.choosingwisely.org/clinician-lists/american-academy-hospice-palliative-care-topical-drugs-for-nausea/. Published 2013. Updated February 21, 2013. Accessed December 8, 2020.

APPENDICES

Appendix 1. Search strategies for bibliographic databases

MEDLINE search strategy

- Platform: Ovid
- Years searched: Ovid MEDLINE and epub ahead of print, in-process and other non-indexed citations and daily 1946 to March 23, 2020
- Date last searched: March 24, 2020
- Limits: Humans (search hedge); English language
- Number of results: 108

1	haloperidol/	15639
2	haloperidol$.tw.	18039
3	or/1-2	22283
4	exp administration, topical/	86627
5	topical$.tw.	103077
6	percutaneous$.tw.	141643
7	cutaneous$.tw.	148817
8	transdermal$.tw.	14278
9	derm$.tw.	237626
10	mucosal$.tw.	118072
11	mucous$.tw.	22634
12	rectal$.tw.	86606
13	emulsions/	17679
14	exp gels/	50757
15	liniments/	122
16	ointments/	12746
17	skin cream/	983
18	suppositories/	3917
19	emulsion?.tw.	32148
20	gel?.tw.	304164

21	liniment?.tw.	143
22	ointment?.tw.	11661
23	salve?.tw.	338
24	paste?.tw.	12162
25	unguent$.tw.	111
26	lotion?.tw.	2265
27	cream?.tw.	18521
28	suppositor$.tw.	4365
29	or/4-28	1219697
30	and/3,29	272
31	exp animals/ not humans/	4681428
32	30 not 31	123
33	limit 32 to english language	108

Embase search strategy

- Platform: Elsevier
- Years searched: 1947 to present
- Date last searched: March 24, 2020
- Limits: Humans (search hedge); English language
- Number of results: 222

1	haloperidol'/mj	22242
2	haloperidol*':ti,ab,tn	23173
3	#1 OR #2	33096
4	topical drug administration'/exp	110771
5	rectal drug administration'/de	8656
6	topical*':ti,ab	146272
7	cutaneous*':ti,ab	213519
8	transdermal*':ti,ab	20815
9	derm*':ti,ab	372207
10	mucosal*':ti,ab	167917
11	mucous*':ti,ab	38200
12	rectal*':ti,ab	137093
13	cream'/de	9180
14	gel'/exp	73480
15	liniment'/de	248
16	lotion'/de	2804
17	ointment'/exp	18376
18	paste'/de	2490
19	salve'/de	165
20	suppository'/de	6013
21	emulsion'/exp	44216
22	cream$':ti,ab	29020

23	emulsion$':ti,ab	43946
24	lotion$':ti,ab	3941
25	ointment$':ti,ab	21285
26	paste$':ti,ab	14635
27	salve$':ti,ab	469
28	suppositor*':ti,ab	7074
29	unguent*':ti,ab	239
30	liniment*':ti,ab	239
31	gel$':ti,ab	357380
32	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31	1528198
33	#3 AND #32	495
34	[animals]/lim NOT [humans]/lim	6007063
35	#33 NOT #34	252
36	#33 NOT #34 AND [english]/lim	222

Appendix 2. Survey instrument for professional medical associations

Welcome. We want to understand your clinical use of compounded haloperidol. 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)	○	○	○
503A Compounding pharmacy (a pharmacy that prepares compounded medications prescribed by practitioners to meet a patient-specific need)	○	○	○
503B Outsourcing facility (a facility that compounds larger quantities without the receipt of a patient-specific prescription)	○	○	○

2. Do you prescribe or administer haloperidol to your patients?

    - Yes
    - No

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

    - Rectal suppository
    - Topical dosage forms (e.g. cream, gel ointment)
    - None of the above

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

    - Agitation
    - Delusional disorders
    - Psychoses
    - Restlessness
    - Schizophrenia
    - Schizoaffective disorder
    - Tourette's
    - Other (please describe) ________

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

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

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

    - Yes
    - No
    - I'm not sure

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

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

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

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

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

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

Appendix 3. Survey instrument

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.