U.S. FOOD & DRUG ADMINISTRATION

MEMORANDUM

TO: File

FROM: Center for Drug Evaluation and Research

DATE: July 29, 2020

SUBJECT: Clinical need for diphenylcyclopropenone (DPCP) in compounding under section 503B of the FD&C Act

This memorandum reflects the discussions of the 503B Working Group, comprised of representatives from the following: CDER Office of New Drugs, Office of Pharmaceutical Quality, Office of Regulatory Policy, Office of Compliance, and Office of Regulatory Affairs

The Food and Drug Administration (FDA or Agency) is developing a list of bulk drug substances that can be used in compounding under section 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 353b). Section 503B of the FD&C Act describes the conditions that must be satisfied for drug products compounded by an outsourcing facility to be exempt from requirements concerning FDA approval prior to marketing (section 505 (21 U.S.C. 355)); labeling of drugs with adequate directions for use (section 502(f)(1) (21 U.S.C. 352(f)(1))); and drug supply chain security requirements (section 582 (21 U.S.C. 360eee-1)).[1]

To qualify for the exemptions available in section 503B of the FD&C Act, a drug product must be compounded in an outsourcing facility that does not compound using bulk drug substances unless: (1) the bulk drug substance appears on a list established by the Secretary of Health and Human Services identifying bulk drug substances for which there is a clinical need (the 503B Bulks List), or (2) the drug compounded from such bulk drug substances appears on the drug shortage list in effect under section 506E of the FD&C Act (21 U.S.C. 356e) at the time of compounding, distribution, and dispensing.

This memorandum evaluates diphenylcyclopropenone (DPCP) for the 503B Bulks List for the treatment of alopecia areata under the "clinical need" standard in section 503B of the Act.

We evaluated DPCP for potential inclusion on the 503B Bulks List under the clinical need standard in section 503B, consistent with the interpretation and policies described in FDA's

[1] In general, drug products compounded under the conditions in section 503B must meet current good manufacturing practice (CGMP) requirements in section 501(a)(2)(B) of the FD&C Act (21 U.S.C. 351(a)(2)(B)). Outsourcing facilities are also subject to FDA inspections according to a risk-based schedule, specific adverse event reporting requirements, and other conditions that help to mitigate the risks of the drug products they compound. Outsourcing facilities may or may not obtain prescriptions for identified individual patients and can, therefore, distribute compounded drugs to healthcare practitioners for "office stock," to hold in their offices in advance of patient need.

March 2019 guidance, "Evaluation of Bulk Drug Substances Nominated for Use in Compounding Under Section 503B of the Federal Food, Drug, and Cosmetic Act" (the Clinical Need Guidance). Because DPCP is not a component of an FDA-approved drug, we did not ask the questions in the Part 1 analysis described in the Clinical Need Guidance. Consistent with the Part 2 analysis in the Clinical Need Guidance, we have considered data and information regarding the physical and chemical characterization of DPCP, safety issues raised by use of this substance in compounding, available evidence of effectiveness or lack of effectiveness, and historical and current use in compounding.[2] **For the reasons stated below, we conclude that the Agency should propose adding the bulk drug substance DPCP to the 503B Bulks List with a limitation for topical use only.**

I. Background

A. Nominated Product

The American Society of Health-System Pharmacists (ASHP) nominated DPCP, at varying concentrations, usually 2 percent for topical use for the treatment of alopecia areata (Docket no. FDA-2013-N-1524, document no. FDA-2013-N-1524-1363). (See Appendix A – ASHP Nomination.) Although the ASHP nomination did not address it, we also considered available safety evidence from the use of DPCP for treatment of non-genital warts because this indication was considered by FDA in the 503A Evaluation.

B. Other Materials Reviewed

In addition to ASHP's nomination for the 503B Bulks List, the Agency considered data and information from its earlier evaluation regarding the use of DPCP for the list of bulk drug substances that can be used in compounding under section 503A of the FD&C Act (21 U.S.C. 353a) (the 503A Bulks List) (the 503A Evaluation). DPCP was nominated for use in compounding drug products under section 503A to treat alopecia areata and nongenital warts. FDA reviewed DPCP in a February 4, 2015 memorandum to the Pharmacy Compounding Advisory Committee (PCAC), which included background materials from a 1999 review of DPCP. (See Appendix B – February 4, 2015 Memorandum.) At its meeting on February 24, 2015, the PCAC voted to include DPCP for topical use on the 503A Bulks List. FDA also consulted with the United States Pharmacopoeia Convention (USP) as part of the Agency's consideration of DPCP for inclusion on the 503A Bulks List.[3] FDA added this substance to the 503A Bulks List with a limitation for topical use only (84 FR 4696).

FDA also considered the report provided by the University of Maryland Center of Excellence in Regulatory Science and Innovation (CERSI) (See Appendix C – CERSI Report on DPCP.) and

[2] In particular, OPQ has reviewed the data and information regarding the physical and chemical characterization of DPCP, OND has reviewed safety issues raised by use of this substance in compounding and available evidence of effectiveness or lack of effectiveness, and Compliance has reviewed information about the historical and current use in compounding.

[3] Materials from the PCAC's 2015 meetings are available on FDA's website at https://wayback.archive-it.org/7993/20170403224128/https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/PharmacyCompoundingAdvisoryCommittee/ucm431285.htm.

conducted a search for relevant scientific literature and safety information, as described below in footnote 6, focusing on materials published or submitted to FDA since the 503A Evaluation.

II. Evaluation

A. Physical and Chemical Characterization

We agree with the conclusion in the February 4, 2015 memorandum to the PCAC that DPCP is well-characterized but degrades readily by basic hydrolysis or exposure to light.[4] The preparation of DPCP has been well developed. Degradation products other than diphenylacetylene have not been identified.

B. Safety Issues Raised by Use of the Substance in Compounding

We agree with the conclusions in the February 4, 2015 memorandum to the PCAC which reviewed nonclinical data and human safety data.

The February 4, 2015 memorandum stated that there has been no systematic evaluation of the toxicology of DPCP to support nonclinical safety.[5] No clinical trials have been specifically conducted to evaluate the safety of DPCP.[6] There is a lack of data on the long-term safety in the use of DPCP. There is also a lack of data on use in specific populations such as pregnant or lactating women.

However, as described in the February 4, 2015 memorandum, over the past several decades safety data have accumulated from uncontrolled studies or case series. The data show that the adverse effects of DPCP are primarily related to its action as contact sensitizer, and the safety profile is probably not worse than those of available products (regardless of FDA approval) in the management of alopecia areata. Because DPCP is a contact sensitizer, there is a concern that handlers of the substance may become inadvertently sensitized and develop contact dermatitis. In addition, more recent reports describe extensive scalp edema, hair becoming curly, actual erythema multiforme major, and vitiligo.

DPCP's mechanism of therapeutic action is through its sensitizing effect which induces allergic contact dermatitis. The reported adverse effects are related to DPCP's mechanism of therapeutic

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[4] See Appendix B – February 4, 2015 Memorandum, at Section II.A.

[5] See Appendix B – February 4, 2015 Memorandum, at Section II.B.1.

[6] See Appendix B – February 4, 2015 Memorandum, at Section II.B.2.

In March and April 2020, a search of the FAERS, CAERS, EMBASE, PubMed, TOXNET, and Google/Google Scholar databases was conducted focusing on materials published or submitted to FDA since the 503A Evaluation. Our determination regarding DPCP's safety and efficacy profile is, indeed, unchanged. The March 2020 FAERS search identified only 12 reports total, 9 of which post-dated the 2014 review. These FAERS reports cannot be directly linked to DPCP use because of concomitantly used medications. Additionally, no reports were retrieved from CAERS. The other sources identified 28 relevant new articles on the use of compounded DCPC for alopecia areata that were not previously considered (see Section IV- Bibliography). The findings in these sources do not alter conclusions reached previously on the use of DCPC compounding for the treatment of alopecia areata.

action as a sensitizer causing allergic contact dermatitis in treated patients. The skin reactions are usually limited in scope and in severity and are generally manageable by the patient without additional medical intervention.

C. Available Evidence of Effectiveness or Lack of Effectiveness

We agree with the conclusion in the February 4, 2015 memorandum to the PCAC that, although there are no adequate and well-controlled trials on DPCP, there appears to be evidence that this substance used in compounding for the treatment of alopecia areata may be useful in some patients.[7] We recognize that treatment with DPCP requires initial sensitization and typical protocols involve a DPCP strength of 2%, but higher concentrations may be used in other patients (see Appendix C – CERSI Report on DPCP). As lack of sensitization is not a safety issue, the nominator has not requested an upper limit for DPCP strength, and we concur.

For treatment of alopecia areata, topical immunotherapy with DPCP provides response rates generally in the order of 50% to 60% but relapses are reported in the majority of patients. The variability of results is attributed primarily to factors like age, disease duration, and severity, but may also be related to the DPCP source and strengths used in the reports. Responses are lower for patients with a younger age of onset, longer duration of disease, and alopecia totalis/universalis.

Because of the amount of evidence accumulated over time, Fitzpatrick's Dermatology in General Medicine (8th edition, 2012) has concluded: "Although not approved by the FDA, topical immunotherapy seems to be the most effective therapeutic option with the best safety profile in the treatment of chronic severe alopecia areata." Currently the topical immunotherapy commonly used in medical practice for these conditions are DPCP and squaric acid dibutyl ester.

D. Historical and Current Use in Compounding

DPCP has been used in pharmacy compounding to treat alopecia areata, and other dermatologic conditions, for over 35 years.[8] The extent of use could not be precisely determined, but in addition to the United States, use of DPCP has been reported in North and South America, Australia, and European and Asian countries.

Information obtained by CERSI from its review of articles, other materials, and interviews supports our assessment of the historical use and suggests a similar profile for the current use of DPCP. Dermatologists interviewed stated that they were not experts in the use of DPCP for alopecia areata but acknowledged DPCP's use for this purpose. The dermatologists interviewed also stated that since sensitization with DPCP typically occurs in the office at a high concentration, "office stock" may be appropriate if the provider treats alopecia areata regularly.

[7] See Appendix B – February 4, 2015 Memorandum, at Section II.C, and footnote 6 above.

[8] See Appendix B – February 4, 2015 Memorandum, at Section II.D.

III. Recommendation

DPCP was nominated as a bulk drug substance for the 503B Bulks List to compound drug products for topical use at variable concentrations, usually 2 percent, in the treatment of alopecia areata.[9] The nominated bulk drug substance is not a component of an FDA-approved drug product. We evaluated DPCP for potential inclusion on the 503B Bulks List under the clinical need standard in section 503B of the FD&C Act, considering data and information regarding the physical and chemical characterization of DPCP, safety issues raised by use of this substance in compounding, available evidence of effectiveness or lack of effectiveness, and historical and current use in compounding.

DPCP is well characterized but there are concerns about stability and consistency in product quality. Although there are still gaps in the evidence for DPCP's safety and effectiveness, including a lack of long-term safety data, substantial human safety data have been collected and clinicians worldwide have gained experience in the use of DPCP to treat alopecia areata. DPCP has been used for several decades to compound drug products for dermatologists to treat alopecia areata and continues to be used for this purpose. The reported adverse effects are related to DPCP's mechanism of therapeutic action as a sensitizer, causing allergic contact dermatitis in treated patients. Alopecia areata may not respond adequately to available treatments. DPCP can be a potentially effective agent for patients who have failed FDA-approved and other therapies for this condition.

On balance, the physical and chemical characterization, safety, effectiveness, and historical and current use of DPCP weigh in favor of including this substance on the 503B Bulks List. Accordingly, we propose adding DPCP to the 503B Bulks List for topical dermal use only. Nominators did not submit, and we have not identified, significant evidence to support use in other routes of administration.

[9] See Docket No. FDA-2013-N-1524, document no. FDA-2013-N-1524-1363.

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APPENDIX SECTION A

September 30, 2014

Division of Dockets Management (HFA-305)
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: FDA-2013-D-1524 Bulk Drug Substances That May Be Used To Compound Drug Products in Accordance with Section 503A of the Federal Food, Drug, and Cosmetic Act, Concerning Outsourcing Facilities; Revised Request for Nominations

Dear Sir/Madam:

The American Society of Health-System Pharmacists (ASHP) is pleased to submit comments to the Food and Drug Administration (FDA) on bulk drug substances that may be used to compound drug products. Nominations for this list were originally announced in the Federal Register on December 4, 2013.[1] A revision to this notification was published on July 2, 2014.[2] This list would fulfill Section 503A of the Federal Food, Drug and Cosmetic Act (FD&C Act) which regulates entities that compound drugs. On November 27, 2013, the Drug Quality and Security Act (DQSA) was signed into law [P.L. 113-54]. The DQSA removed several parts of Section 503A that were declared unconstitutional by the U. S. Supreme Court in 2002. The law requires the FDA to go through the rulemaking process to implement several parts of Section 503A, including a requirement to establish a list of bulk drug substances that may be used in compounding for which there is no applicable USP or NF monograph nor are they components of an FDA-Approved drug.

ASHP represents pharmacists who serve as patient care providers in acute and ambulatory settings. The organization's more than 40,000 members include pharmacists, student pharmacists and pharmacy technicians. For over 70 years, ASHP has been on the forefront of efforts to improve medication use and enhance patient safety. As you are well aware, ASHP was

1 Federal Register, Volume 78, No. 233. Pages 72838 –72840
2 Federal Register, Volume 79, No. 127. Pages 37750–37754

actively engaged with the FDA and Federal lawmakers from the onset of the meningitis outbreak in the Fall of 2012. In the aftermath of the incident, ASHP has worked with policymakers, practitioners, and nationally recognized experts in compounding and manufacturing to develop new approaches to protect patients from preventable harm, and to give practitioners and organizations confidence that compounding outsourcers are appropriately regulated and inspected, and that the products they produce are safe.

ASHP understands that the FDA received thousands of nominations for substances to be included on the bulk list, but that the overwhelming majority of nominations did not meet the basic definition of "active ingredient," and will therefore not be considered by the FDA. Further, the Agency states "Bulk substances that were previously nominated will not be further considered unless they are renominated and adequately supported." ASHP previously submitted comments to the FDA under the original solicitation for bulk substances and we are again nominating three chemicals – diphenylcyclopropenone, squaric acid dibutyl ester, and thymol iodide – for consideration by the FDA. Please see the accompanying excel file which contains a worksheet for each of the drugs with the information outlined by the FDA.

ASHP appreciates the opportunity to comment as the FDA develops a list of bulk drug substances that may be used in compounding. Please contact me if you have any questions or wish to discuss our comments further. I can be reached by telephone at 301-664-8806, or by e-mail at ctopoleski@ashp.org.

Sincerely,

Christopher J. Topoleski
Director, Federal Regulatory Affairs.

Column A—What information is requested?	Column B—put data specific to the nominated substance	References
What is the name of the nominated ingredient?	Diphenylcyclopropenone	http://crs.edqm.eu/db/4DCGI/web_catalog_CRS http://crs.edqm.eu/
Is the ingredient an active ingredient that meets the definition of “bulk drug substance” in § 207.3(a)(4)?	Yes	
What is the chemical name of the substance?	2,3-DIPHENYL-2-CYCLOPROPEN-1-ONE (C15H10O)	http://fdasis.nlm.nih.gov/srs/ProxyServlet?mergeData=true&objectHandle=DBMaint&APPLICATION_NAME=fdasrs&actionHandle=default&nextPage=jsp/srs/ResultScreen.jsp&TXTSUPERLISTID=I7G14NW5EC&QV1=DIPHENYLCYCLOPROPENONE
What is the common name of the substance?	DIPHENCYPRONE	http://fdasis.nlm.nih.gov/srs/ProxyServlet?mergeData=true&objectHandle=DBMaint&APPLICATION_NAME=fdasrs&actionHandle=default&nextPage=jsp/srs/ResultScreen.jsp&TXTSUPERLISTID=I7G14NW5EC&QV1=DIPHENYLCYCLOPROPENONE
Does the substance have a UNII Code?	I7G14NW5EC	http://fdasis.nlm.nih.gov/srs/ProxyServlet?mergeData=true&objectHandle=DBMaint&APPLICATION_NAME=fdasrs&actionHandle=default&nextPage=jsp/srs/ResultScreen.jsp&TXTSUPERLISTID=I7G14NW5EC&QV1=DIPHENYLCYCLOPROPENONE
What is the chemical grade of the substance?	Description, melting point, purity meets technical grade standards	http://datasheets.scbt.com/sds/WPNA/EN/sc-255115.pdf
What is the strength, quality, stability, and purity of the ingredient?	Varies - Ex: 1 gm and 5gm in glass bottle; 98% purity; stable if stored in dry, well-ventilated place	http://www.sigmaaldrich.com/MSDS/MSDS/DisplayMSDSPage.do?country=US&language=en&productNumber=177377&brand=ALDRICH&PageToGoToURL=http%3A%2F%2Fwww.sigmaaldrich.com%2Fcatalog%2Fproduct%2Faldrich%2F177377%3Flang%3Den
How is the ingredient supplied?	Crystalline Powder, Powder or Crystals	http://www.sigmaaldrich.com/MSDS/MSDS/DisplayMSDSPage.do?country=US&language=en&productNumber=177377&brand=ALDRICH&PageToGoToURL=http%3A%2F%2Fwww.sigmaaldrich.com%2Fcatalog%2Fproduct%2Faldrich%2F177377%3Flang%3Den

Is the substance recognized in foreign pharmacopeias or registered in other countries?	No	http://crs.edqm.eu/db/4DCGI/web_catalog_CRS http://www.pharmacopoeia.co.uk/pdf/BP_2015_Index.pdf http://www.pmda.go.jp/english/pharmacopoeia/pdf/jpdata/JP16eng.pdf
Has information been submitted about the substance to the USP for consideration of monograph development?	Unknown; no current monograph available	USP-NF
What medical condition(s) is the drug product compounded with the bulk drug substances intended to treat?	Treatment of extensive alopecia aerate	https://www.medicinescomplete.com/mc/martindale/current/4896-w.htm?q=diphenylcyclopropenone&t=search&ss=text&p=1#_hit
Are there other drug products approved by FDA to treat the same medical condition?	Yes	
If there are FDA-approved drug products that address the same medical condition, why is there a clinical need for a compounded drug product?	Possibly due to limited topical options in treating alopecia aerate	http://www.ncbi.nlm.nih.gov/pubmed/20115946
Are there safety and efficacy data on compounded drugs using the nominated substance?	Yes; limited to conducted studies, best information based on review article	http://www.ncbi.nlm.nih.gov/pubmed/20115946
If there is an FDA-approved drug product that includes the bulk drug substance nominated, is it necessary to compound a drug product from the bulk drug substance rather than from the FDA-approved drug product?	No	http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm
What dosage form(s) will be compounded using the bulk drug substance?	Topical Solution	
What strength(s) will be compounded from the nominated substance?	Varies; usually 2%	Journal of the American Academy of Dermatology; Volume 44, Issue 1, January 2001, Pages 73–76
What are the anticipated route(s) of administration of the compounded drug product(s)?	Topically	
Has the bulk drug substance been used previously to compound drug product(s)?	Yes	
Is there any other relevant information?	Pubmed Search Results:	http://www.ncbi.nlm.nih.gov/pubmed?cmd=search&cmd_current=Limits&term=Diphenylcyclopropе

		none+OR+886-38-4+%5Brn%5D
	MSDS:	http://www.sigmaaldrich.com/MSDS/MSDS/DisplayMSDSPage.do?country=US&language=en&productNumber=177377&brand=ALDRICH&PageToGoToURL=http%3A%2F%2Fwww.sigmaaldrich.com%2Fcatalog%2Fproduct%2Faldrich%2F177377%3Flang%3Den
	CAS:	886-38-4

APPENDIX SECTION B

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993-0002

DATE: February 4, 2015

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TO: Pharmacy Compounding Advisory Committee

SUBJECT: Review of Diphenylcyclopropenone for Inclusion on the 503A Bulk Drug Substances List

I. Introduction

Diphenylcyclopropenone (DPCP) has been nominated for inclusion on the list of bulk drug substances for use in compounding under section 503A of the Federal Food, Drug, and Cosmetic Act (FD&C Act). Indications identified in the nomination include the treatment of non-genital warts and alopecia areata. FDA reviewed this substance in 1999, and it is now being reevaluated. The background materials from the prior review are attached.

We have reviewed the physicochemical characteristics, safety, effectiveness, and historical use in compounding of this substance. Based on those factors, for the reasons discussed below, we recommend that DPCP be added to the list of bulk drug substances that can be used to compound drug products in accordance with section 503A of the FD&C Act.

II. EVALUATION CRITERIA

A. Is the substance well-characterized, physically and chemically, such that it is appropriate for use in compounding?

1. Stability of the API and likely dosage forms

According to FDA's 1999 assessment, attached, "The physical and spectroscopic properties of DPCP are well-characterized. DPCP is insoluble in water, soluble in alcohols and other organic solvents, and is rapidly hydrolyzed in dilute alcoholic base. DPCP reacts with nucleophiles, such as pyridine and hydroxylamine, to form a variety of unidentified products. Thermal instability has been reported. Heating this material above its melting point results in decomposition to diphenylacetylene and carbon monoxide. DPCP reacts photochemically to ultraviolet (UV-A and UV-B), fluorescent, and incandescent lights, as well as natural sunlight. There are no published quantitative methods for analysis of this material. The adequacy of the methods for determination of purity and levels of contaminants cannot be assessed."

DPCP has been found "to decompose, forming diphenylacetylene on exposure to both sunlight and fluorescent light in less than 2 weeks. Samples shielded from the light at -70° C and at room temperature were stable over a 4-week period. The extent of decomposition was the same in both ethanol and cyclohexane. It is possible that DPCP may act as a prosensitizer with the actual sensitizer liberated by a photoactivated intermediate (stable, metastable, or unstable) or a combination of these" (Wilkerson et al., 1984). It has further been reported on the DermNet NZ website that "DPCP is made up in acetone. It should be stored in a dark glass bottle in a cupboard away from sunlight and kept secure from access by children. The compounded preparation has a shelf-life of around 6 months."

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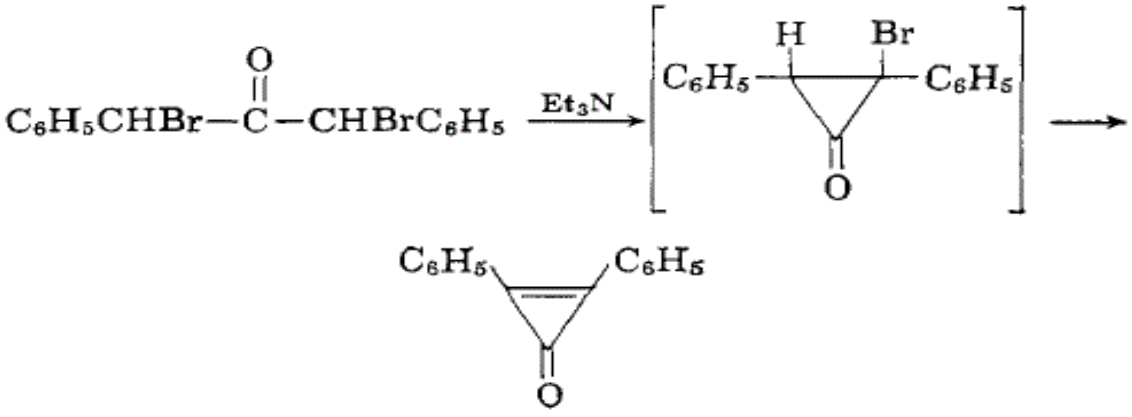
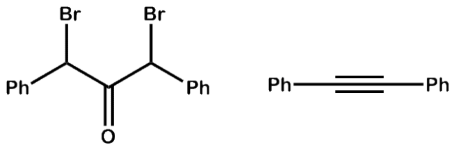


2. Probable routes of API synthesis

Breslow reports that "Diphenylcyclopropenone may be synthesized by a variety of methods; the best procedure involves elimination of HBr from α,α'-dibromodibenzyl ketone,…" (Breslow et al,. 1965).

3. Likely impurities

The likely impurities are the starting material, α,α'-dibromodibenzyl ketone, and the degradation product diphenylacetylene.



Breslow reports that DPCP is a crystalline solid with a melting point of 119° to 120° C. If the material is purified by recrystallization to this melting point, it is likely that the starting α,α'-dibromodibenzyl ketone is present in no more than a few tenths of a percent. (Breslow et al,. 1965).

4. Toxicity of those likely impurities

Note that α,α'-dibromodibenzyl ketone contains a structural alert for mutagenicity. It is reported on the DermNet NZ website that "[a]lthough DPCP is non-mutagenic in the Ames test, its precursor and possible contaminant during commercial production, α,α'-dibromodibenzyl ketone, can be mutagenic."

However, Wilkerson found no detectable contaminants in their analysis of commercial DPCP (Wilkerson et al., 1984).

Specific toxicity concerns are addressed below in the **Nonclinical Assessment** section.

5. Physicochemical characteristics pertinent to product performance, such as particle size and polymorphism

As DPCP is used in solution, there are no concerns related to particle size or polymorphism.

Conclusions: We concur with FDA's 1999 assessment that "[a]lthough DPCP is well characterized, it degrades readily by basic hydrolysis or exposure to light. The degradation products [other than diphenylacetylene] have not been identified. DPCP used in compounding

could vary significantly from DPCP used in literature studies in the level and types of impurities present; this could result in altered clinical properties and toxicities."

B. Are there concerns about the safety of the substance for use in compounding?

1. Nonclinical Assessment

a. Pharmacology of the drug substance

DPCP is a hapten that is capable of eliciting contact dermatitis. Following repeated topical applications to the ears of mice, DPCP was found to induce local and systemic immune responses that included immune cell proliferation and altered cytokine activity (Svalgaard et al., 2014).

b. Safety pharmacology

No information available.

c. Acute toxicity

No information available.

d. Repeat dose toxicity

No information available

e. Mutagenicity

DPCP was considered not mutagenic in a reverse mutation assay conducted with bacteria (Wilkerson et al., 1987). Mammalian genotoxicity data have not been located within the public domain.

f. Developmental and reproductive toxicity

No information available.

g. Carcinogenicity

No information available.

h. Toxicokinetics

No information available.

Conclusions: There has been no systematic evaluation of the toxicology of DPCP to support nonclinical safety.

2. Human Safety

a. Reported adverse reactions

There are no randomized controlled trials for DPCP use. Since estimated adverse reaction rates from case reporting and unblinded studies can be misleading, they will not be discussed. Case reporting comes from populations of uncertain size while bias in unblinded studies cannot be eliminated, making estimation of adverse reaction rates unreliable.

DPCP is a contact sensitizer, and the expected manifestations of contact sensitization have been amply reported, including, for example, severe local eczematous reactions, erythema, pruritus, blisters, and burning. There have also been reports of hypopigmentation and lymphadenopathy, as well as erythema multiforme-like eruption and contact urticaria. These have been well documented in publications by van der Steen et al., (1991), Perret et al., (1990) and Tosti et al. (1989).

b. Clinical trials assessing safety

The human safety data up to 1999 have been summarized in FDA's review of DPCP for the Pharmacy Compounding Advisory Committee in that year (see attached). The information therein is consistent with the adverse reaction profile described above in Section II.B.2.(a). No clinical trials have been specifically conducted to evaluate the safety of DPCP. The human safety data are derived primarily from uncontrolled studies or case series.

Over the past 15 years (1999 to 2014), there have been additional reports of non-genital wart treatment with DPCP in otherwise healthy and in immunocompromised patients (Upitis and Krol 2002, Boull and Groth 2011, Audrain et al., 2013), with the adverse reaction profile showing primarily contact dermatitis manifestations and no new local or systemic findings. The case is similar with alopecia areata (Avgerinou et al., 2008, Chiang et al., 2014).

c. Pharmacokinetic data

The potential for absorption of DPCP is not clear. Even though in the only reported study (Berth-Jones et al.) DPCP was not detected in the serum or urine, the limit of detection in these biological samples was high; thus there might have been DPCP present at levels below the limit of detection. In addition, it is possible that the DPCP was absorbed and metabolized, thus rendering it not measurable.

In the reported study, Berth-Jones et al., applied a minimum of 0.5 ml (actual volume not described) of a solution containing 1% (w/v) DPCP to the scalp. Single blood samples were obtained from 7 subjects at 30 – 60 minutes after application and complete blood profile (at 15, 30, 60, 90 minutes, 2, 4 and 8 hours after application) was obtained in another 7 subjects; 24-hour urine collections were obtained from 6 subjects. DPCP was

not detected in any serum or urine sample from any subject. The authors noted that at the limit of detection, they should have been able to detect presence of 0.3 – 0.9% of the applied dose if it was excreted in the urine unchanged.

d. The availability of alternative approved therapies that may be as safe or safer

The more common alopecia areata therapies include intralesional corticosteroid injection, topical corticosteroids, minoxidil, anthralin, phototherapy, systemic corticosteroids, cyclosporine, sulfasalazine, and methotrexate. However, the only FDA-approved therapy indicated for the treatment of alopecia areata is intralesional injection of corticosteroid suspensions, including triamcinolone acetonide, triamcinolone hexacetonide, betamethasone acetate and betamethasone sodium phosphate, and methylprednisolone acetate products. This form of treatment carries the risk of permanent skin atrophy with repeated injections.

Contact sensitizer therapy is usually reserved for use on cutaneous warts resistant to more regular treatment modalities. Such warts are frequently treated via initial physical destruction with cryotherapy and paring or excision. Topical salicylic acid in different vehicles has been included in the over-the-counter monograph, Wart Remover Drug Products (21 CFR 358 subpart B). There are no approved therapies for recalcitrant warts not responding to the above (e.g., cryotherapy, topical salicylic acid).

For the treatment of genital warts, approved drugs include podofilox gel and solution, imiquimod cream, and polyphenon E ointment. Solicitation of a contact dermatitis reaction in the skin of the genital area with sensitizers poses additional challenges for management, because it may be more difficult to treat the eczematous reaction there and it may also enhance the risk of secondary infections in this location. This makes the use of DPCP not desirable for the treatment of genital warts.

Conclusions: Although DPCP is not mutagenic in the Ames assay, there are inadequate nonclinical data to otherwise characterize its safety profile. However, much clinical safety data have accumulated over the past 30 to 40 years. They show that the adverse effects of DPCP are primarily related to its action as contact sensitizer, and the safety profile is probably not worse than those of available products (regardless of FDA approval) in the management of alopecia areata and recalcitrant warts. No additional safety issues have been discovered in the past 15 years since the last review by the Committee. Nevertheless, there is a lack of data on the long-term safety in the use of DPCP.

Because DPCP is a contact sensitizer, there is a concern that handlers of the substance may become inadvertently sensitized and develop contact dermatitis.

There is also a lack of data on use in specific populations such as pregnant or lactating women. Although systemic absorption of DPCP is probably low, the exposure of and risks to the fetus and neonates being nursed are unknown. At the University of British Columbia Hair Clinic, six women have become pregnant while on treatment with DPCP despite the fact that they were

warned and signed an informed consent. However, all babies born were apparently normal (Alkhalifah et al., 2010).

C. Are there concerns about whether the substance is effective for a particular use?

1. Reports of trials, clinical evidence, and anecdotal reports of effectiveness, or lack of effectiveness, of the bulk drug substance

Non-genital Warts

Reference is made to FDA's review on effectiveness data on DPCP in the treatment of cutaneous warts in 1999, which summarized the available data at that time. FDA noted that the largest trial with DPCP on warts was an open-label study in 134 subjects in which 60% of subjects had complete or partial responses after 8 weeks of treatment (Rampen and Steijlen, 1996).

Between 1999 and 2014, there have been many additional reports of the use of DPCP in the treatment of non-genital warts. Although these are not randomized, placebo-controlled, double-blind trials, they do provide evidence from a much larger treated population to support effectiveness of DPCP in recalcitrant warts.

- It appears that the largest series during this period is that from Upitis and Krol (2002) with 211 patients who had recalcitrant warts achieving a complete clearance rate of 88%.
- Boull and Groth's review of cutaneous viral warts in children included 143 patients treated with DPCP showing cure rates of 88% and 63% in two studies (Buckley et al., 1999 [not included in FDA's review of 1999] and Choi et al., 2008 [which also included a cryotherapy control with cure rate of 51%], respectively).
- In 2013, Choi et al., reported a series of 27 DPCP-treated patients with periungal warts showing complete clearance rate of 85% by subject (52% of them being failures with other treatments) and 91% by lesion.
- Audrain and Siddiqui (2013) obtained cure rates for recalcitrant warts of 96% in 28 immunocompetent and 60% in 10 immunosuppressed patients treated with DPCP.

Alopecia Areata

Reference is made to FDA's review on effectiveness data on DPCP in the treatment of alopecia areata in 1999, which summarized the available data at that time, citing reports by Schuttellaar et al., (1996), Gordon et al., (1996), Shapiro et al., (1993), van der Steen et al., (1991) and Berth-Jones et al., (1994), which gave response rates between 9% to 50%.

Williams and Bigby's 2014 edition of Evidenced-Based Dermatology states:

> Schuttlelaar et al., treated 26 children with diphencyprone weekly for a period of 3-12 months. Sixteen subjects had alopecia areata totalis, and the others had patchy disease only. Eighty-four percent of the children showed hair regrowth, 32% of the total being cosmetically acceptable. Where treatment failed (0-5% hair growth), it was recommended not to continue treatment for longer than 1 year, as hair growth is not promoted by continued treatment.

In 2013, Shapiro summarized the literature experience, noting that topical immunotherapy of alopecia areata with squaric acid dibutyl ester and DPCP (13 trials and 17 trials, respectively) gave similar results: success rate of 50 to 60% with a wide range of 9 to 87%. This is generally dependent on the severity and duration of disease and the heterogeneity of product source, but it is also possible that the variability is related to the compounding with a wide range of strengths used in treatment. Relapse after achieving significant regrowth develops in the majority of patients, with median time to relapse of 2½ years.

2. Whether the product compounded with this bulk drug substance is intended to be used in a serious or life-threatening disease

The intended use of products compounded with DPCP has included treatment of severe forms of alopecia areata and recalcitrant cutaneous warts. These are not serious or life-threatening conditions.

3. Whether there are any alternative approved therapies that may be as effective or more effective

The only FDA-approved therapy indicated for the treatment of alopecia areata is intralesional injection of corticosteroid suspensions (see above, Section II.B.2.(d)). This form of therapy is not practical when the alopecia is widespread, as in the case of alopecia totalis or alopecia universalis, because each injection only produces a tuft of hair regrowth of approximately 0.5 cm^2. In addition, alopecia areata is also treated off-label with topical corticosteroids, minoxidil, anthralin, phototherapies, systemic corticosteroids, cyclosporine, sulfasalazine, or methotrexate.

There are approved therapies for non-genital cutaneous warts, but the contact sensitizers are generally reserved for the treatment of recalcitrant warts failing other treatment modalities, and as such, there are no approved alternative therapies for recalcitrant warts.

For the treatment of genital warts, there are approved drugs (podofilox gel and solution, imiquimod cream, and polyphenon E ointment) while solicitation of a contact dermatitis reaction in the treatment area with sensitizers poses additional challenges for management, making the use of DPCP not desirable (see above, Section II.B.2.(d)).

Conclusions: Although there are no adequate and well-controlled trials on DPCP, there appears to be evidence that this substance used in compounding for the treatment of recalcitrant warts and alopecia areata may be effective in a proportion of patients.

For non-genital cutaneous warts, DPCP treatment of recalcitrant cases is able to achieve cure rates between 60% to over 90%.

For alopecia areata treatment, topical immunotherapy with DPCP provides response rates generally in the order of 50% to 60% but relapses are reported in the majority of patients. The variability of results is attributed primarily to factors like age, disease duration, and severity, but may also be related to the DPCP source and strengths used in the reports. Responses are lower for patients with a younger age of onset, longer duration of disease, and alopecia totalis/universalis.

Because of the amount of evidence accumulated over time, Fitzpatrick's *Dermatology in General Medicine* (8th edition, 2012) has concluded: "Although not approved by the FDA, topical immunotherapy seems to be the most effective therapeutic option with the best safety profile in the treatment of chronic severe alopecia areata." Currently the topical immunotherapy commonly used in medical practice for these conditions are DPCP and squaric acid dibutyl ester.

D. Has the substance been used historically in compounding?

1. Length of time the substance has been used in pharmacy compounding

DPCP has been reported for use for over 30 years in pharmacy compounding.

2. The medical condition(s) it has been used to treat

DPCP has been reported for use primarily in the treatment of warts and alopecia areata (including alopecia totalis and alopecia universalis). There are also reports for use in oncology indications, such as melanoma metastases.

3. How widespread its use has been

Use of DPCP has been reported in North and South America, Australia, and European and Asian countries. In 2006, Europe's Committee for Medicinal Products for Human Use (CHMP) granted DPCP orphan designation for the indications alopecia totalis and alopecia universalis to a French firm, Orfagen. Designation was withdrawn in July 2013 at the firm's request.

4. Recognition of the substance in other countries or foreign pharmacopeias

Although DPCP is recognized globally in many countries, a search did not find this substance listed in the European, British, or Japanese Pharmacopeias.

Conclusions: DPCP has been used for compounding to treat resistant non-genital warts and alopecia areata by practitioners for over 30 years. Reports of its global use for these conditions have accumulated over time. There may also be novel uses such as for metastatic melanoma, but this is still under study and considered premature.

III. RECOMMENDATION

We recommend DPCP be placed on the list of bulk drug substances in compounding under section 503A. Despite some concerns about stability and consistency in product quality, as well as lack of adequate nonclinical data, the substance has been in use for compounding for over 30 years and has been adopted globally as a potentially useful form of topical immunotherapy for alopecia areata and recalcitrant warts by medical practitioners. Thus far, the adverse effects reported are related to its primary therapeutic effect as a contact sensitizer.

There are some gaps in knowledge about long-term safety and use in specific populations such as pregnant and lactating women. However, given the lack of approved therapies indicated for recalcitrant warts and severe forms of alopecia areata (alopecia totalis and alopecia universalis), not listing DPCP could create obstacles to patient access, unless the drug product is obtained through an investigational new drug application.

In FDA's review of DPCP in 1999, the primary concern was inadequate safety information, but the reviewers recognized that DPCP might be "useful as second or third line therapy for warts and possibly as a therapy for alopecia areata." Since that time, many more human safety data have been collected, and effectiveness experience in the treatment of severe forms of alopecia areata (alopecia totalis and alopecia universalis) and recalcitrant warts has been gained by clinicians worldwide. This has led to textbooks in dermatology naming this form of therapy as the most effective therapeutic option with the best safety profile in the treatment of such conditions. We believe that it is now appropriate to include DPCP on the 503A bulk drug substances list.

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DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration, Center for Drug Evaluation and Research
Division of Dermatologic and Dental Drug Products, HFD-540

Date: March 16, 1999

Subject: Review of Diphencyclopropenone, a Candidate for the Pharmacy Compounding Bulk List, With Selected References

To: Pharmacy Compounding Steering Committee

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HFD-540 Review on Diphenylcyclopropenone

For the FDA Pharmacy Compounding Advisory Committee

Prepared by: Paul C. Brown, Ph.D.
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Date prepared: January 4, 1999
Revised: March 26, 1999

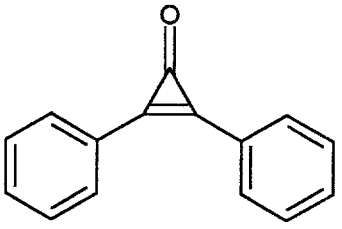
I. Introduction

The Division of Dermatologic and Dental Drug Products (HFD-540) has been charged with the review of diphenylcyclopropenone (DPCP) for two indications: alopecia areata and verruca vulgaris (warts). Only published literature was used in the preparation of this review.

II. Chemical Characterization of DPCP

Identity:

Diphenylcyclopropenone
Diphencyprone
2,3-Diphenyl-2-cyclopropen-1-one
DPCP



CAS #: *886-38-4*
Molecular Weight: *206.24*
Molecular Formula: $C_{15}H_{10}O$
Melting Point: *119-121° C (anhydrate); 87-90° C (monohydrate)*

The physical and spectroscopic properties of DPCP are well-characterized. DPCP is insoluble in water, soluble in alcohols and other organic solvents, and is rapidly hydrolyzed in dilute alcoholic base. DPCP reacts with nucleophiles, such as pyridine and hydroxylamine, to form a variety of unidentified products. Thermal instability has been reported. Heating this material above its melting point results in decomposition to diphenylacetylene and carbon monoxide. DPCP reacts photochemically to ultraviolet (UV-A and UV-B), fluorescent and incandescent lights, as well as natural sunlight. There are no published quantitative methods for analysis of this material. The adequacy of the methods for determination of purity and levels of contaminants cannot be assessed.

Quality and Stability

DPCP is an off-white to beige crystalline powder and has a melting point of 119-121° C. It is thermally unstable above its melting point, decomposing primarily into diphenylacetylene and a possible dimeric product; this degradant has not been definitively identified. It is insoluble in water, readily hydrolyzed in dilute alkali base ($t_{1/2}$ < 5 min. in 0.1N NaOH in ethanol) to cis-1,2-diphenylacrylic acid, and relatively stable to acidic conditions. DPCP reacts readily with strong electrophiles, as well as with nucleophiles such as pyridine and hydroxylamine. The addition products of these reactions have not been fully identified.

DPCP is photochemically reactive. It decomposes during irradiation with both short- and long-wavelength UV (UVB and UVA), fluorescent, incandescent and solar light. The predominant decomposition products appear to be diphenylacetylene and a product which has tentatively been identified as a dimer.

Synthesis and Purity

DPCP was first prepared in 1959 by Breslow (Breslow et al., 1959) and Vol'pin (Vol'pin et al., 1959). Several methods of preparation have been reported in the chemical literature (Breslow et al., 1959, 1963, 1965, 1973; Vol'pin et al., 1959, 1960), only one of which appears amenable to large-scale production (Breslow et al., 1973).

Several domestic commercial sources of DPCP have been identified, including Fisher Scientific (Acros Organics), Spectrum Chemical Co., and Sigma-Aldrich Co. Each has confirmed their knowledge of the identity or identities of the actual manufacturing site(s) for DPCP, but all of them have declined to make this information public.

Literature on the syntheses of DPCP predates modern analytical methodology. These reports cite IR spectroscopy, UV spectroscopy, elemental analysis, and melting point as the determinants of purity. While these methods are common analytical techniques, they are not established quantitative methods for analysis of this material. The adequacy of these methods for determination of the purity and level of contaminants in DPCP can not be assessed.

A monohydrate form of DPCP (melting point 87°-90°C) results from recrystalization in cyclohexane and is probably due to incomplete drying. The reported yield of this synthesis is 44%. The description of the purification indicates the presence of significant amounts of unidentified byproducts (e.g., a "reddish oily impurity"); thus, the impurity profile of this material is unknown.

Assessment 1: Although DPCP is well characterized, it degrades readily by basic hydrolysis or exposure to light. The degradation products have not been identified. DPCP used in compounding could vary significantly from DPCP used in literature studies in the level and types of impurities present; this could result in altered clinical properties and toxicities.

III. Safety of DPCP

A. Animal Toxicology

DPCP is not mutagenic in the Ames assay except in the presence of light (Wilkerson et al., 1987). In the presence of light (350 nm) and rat microsomes, DPCP caused a doubling of the mutation rate in one strain of *Salmonella*. Since the photo-conversion products of DPCP were not mutagenic, some short-lived intermediate(s) must cause the mutations. The synthetic precursor to DPCP, α,α-dibromodibenzylketone, is mutagenic in the Ames assay with and without metabolic activation (Wilkerson et al., 1987).

Assessment 2: DPCP is photo-genotoxic. Mammalian genotoxicity, chronic toxicity, reproductive toxicity, and carcinogenicity studies have not been conducted with DPCP. Thus, it is not known what the potential toxicities of DPCP are in humans or whether it is likely to be teratogenic in humans.

B. Human Safety

There are no published reports of studies designed to systematically evaluate the safety of DPCP. The reported side effects are similar to those of other contact sensitizers. Numerous case reports of adverse events are associated with the use of DPCP. Especially notable are reports of vitiligo and pigmentary changes, some of which are permanent. There have been three reports of erythema multiforme (which is characterized by the appearance of purpuric [bruise-like], often blistering, ring-shaped lesions scattered over the body surface, with systemic signs and symptoms including fever and malaise).

DPCP has been shown to elicit eczematous reactions with or without blistering. These reactions may occur at the site of application and other areas of the body. Other reactions include itching and resulting insomnia, urticaria, edema of the scalp, eyelids, and face, lymphadenopathy, and high fever (Rokhsar et al., 1998).

Table 1 - Side Effects of DPCP

Author	Journal	Year	Side Effect
Alam et al.	J. Am. Acad. Dermatol.	1999	Severe urticarial reaction, eczematous dermatitis, and dermographism
Oh et al.	Contact Derm.	1998	Bullous erythema multiforme
Henderson et al.	Br. J. Dermatol.	1995	Vitiligo
Puig et al.	Int. J. Dermatol.	1994	Erythema multiforme-like reaction
Van der Steen et al.	Arch. Dermatol.	1992	Pigmentation changes (4/243 pts) – 'dyschromia in confetti'
Duhra et al.	Br. J. Dermatol.	1990	Persistent vitiligo
Perret et al.	Dermatologica	1990	Erythema multiforme (3 patients)
Tosti et al.	Contact Derm.	1989	Contact urticaria

In human skin absorption studies, DPCP was not detected in the serum or urine of human subjects treated with 0.5 ml of 1% DPCP in a mixture of denatured alcohol and propylene glycol in a 9:1 ratio for a total dose of 5 mg (Berth-Jones et al., 1994). The limit of detection in this study was 60 ng/ml for serum and 20 ng/ml for urine. The authors note that their results do not eliminate the possibility that DPCP is absorbed and rapidly metabolized.

Topical sensitizers such as DPCP present a particular hazard to those who work with the compounds since, by definition, repeated exposure is likely to elicit an allergic response. There are several published accounts of workers, including pharmacists and nurses, becoming sensitized to DPCP (Sansom et al., 1995; Shah et al., 1996; Adisesh et al., 1997).

Assessment 3: There is limited characterization of the human safety profile. With human exposure to DPCP, adverse side effects have been reported in the literature, including erythema multiforme, eczematous dermatitis, urticaria, persistent vitiligo and post-inflammatory pigmentation changes.

Available alternative approved therapies for alopecia areata include intralesional, topical, and systemic corticosteroids.

Available alternative approved therapies for verruca vulgaris (warts) include podophyllin, imiquimod, and salicylic acid. Other well-accepted modalities with excellent safety include ablation using cryotherapy or laser treatment.

Assessment 4: Many approved products are available for the treatment of verruca and alopecia areata.

IV. Historical Use of DPCP in Pharmacy Compounding

DPCP's ability to induce strong allergic reactions was first reported in 1972 (Whittaker, 1972). Clinical use of DPCP for the treatment of alopecia areata was first reported in 1983 (Happle et al. , 1983).

Numerous animal and human studies have demonstrated that DPCP is a potent contact sensitizer. It has been investigated for topical immunotherapy of conditions such as warts and alopecia areata. The mechanism by which topical immunotherapy can improve these conditions is not known, however exposure of patients to this agent results in a clinical picture similar to that of exposure to poison ivy.

DPCP is usually applied in a health care provider's office by a physician (usually a dermatologist), podiatrist, or trained staff member. First, patients are sensitized with a 2% DPCP solution in acetone applied to a 10 to 16 cm^2 area on one side of the scalp, forearm, or back (Rokhsar et al., 1998). If a severe eczematous response does not occur at the initial sensitization site, a 0.0001% solution is applied to one side of the scalp (if the initial reaction is too severe, two

weeks are allowed to elapse between the sensitization and elicitation phases). Caution must be exercised to avoid a severe blistering response.

Assessment 5: Since its first clinical report in 1983, DPCP has been used as an experimental treatment alternative for alopecia areata and verruca vulgaris. Evidence of its widespread use is not apparent.

V. Available Evidence of Effectiveness

Alopecia areata and warts frequently resolve without any therapeutic intervention. For example, in a study of the natural history of alopecia areata, of 63 alopecia areata patients followed for one year without treatment, hair had regrown in all but 4 patients in one year, and in all but 1 patient after two years. The great majority had regrown hair by 3 months after their only office visit (Arnold, 1952). Alopecia areata with less than 25% involvement has a high incidence of spontaneous recovery, whereas more severe involvement has a lesser rate of recovery (Moschella and Hurley, 1992). Regarding the natural history of warts, a two-year study showed that two-thirds of warts regressed without treatment (Massing and Epstein, 1963).

Despite the necessity for a placebo arm in evaluating experimental therapies such as DPCP, much of the putative success of topical immunomodulators stems from studies that were either uncontrolled or internally controlled. Describing therapy for alopecia areata, Rook et al. states, "The widely conflicting claims for the success of many different measures merely reflect the very great variations in the spontaneous course of the disease."

Studies that demonstrate a "positive" result, such as regrowth of hair, are more likely to be submitted for publication or published than are studies with "negative" results. Therefore, the published literature may overstate the efficacy of novel therapies. Additionally, most clinical studies lack long-term follow-up, so the lasting treatment benefits cannot be evaluated.

To date, in the peer-reviewed English-language literature, there have been at least 18 reports of studies using DPCP in alopecia areata and 5 studies on the treatment of warts.

Warts

Warts, caused by cutaneous infection with the human papillomavirus, are a very common dermatological ailment. Aside from cosmetic disfigurement, patients seek treatment because plantar (foot) warts may cause pain on walking or interfere with gait, and warts on the fingers may interfere with manual dexterity. As with alopecia areata, therapy is not always effective.

The largest trial with DPCP on warts was an open study on 134 subjects with palmoplantar and periungual verruca done by Rampen and Steijlen in 1996. After 8 weeks of treatment, 36.6% of subjects exhibited a complete response. The low rate of response is worse than that of other therapeutic modalities for warts, although the absence of a control arm precludes any definitive comparisons with other modalities.

Alopecia areata

Alopecia areata is a nonscarring loss of hair, that, depending upon its severity, can affect patches of scalp, the entire scalp (alopecia totalis), or the entire body (alopecia universalis). The etiology of this illness is unknown. Alopecia areata is a relatively common dermatologic disease that is associated with cosmetic disfigurement and functional impairment, especially if eyebrows or eyelashes are lost.

Table 2 - Use of DPCP in Alopecia Areata

Author	Journal	Year	Disease	N	Treatment	Response/ITT	Ctrl
Schuttelaar et al.	Br. J. Dermatol.	1996	Alopecia areata Children	26	3 mo – 1 yr	30.8% acceptable regrowth	Yes
Gordon et al.	Br. J. Dermatol.	1996	Alopecia areata	48	30.8 months follow-up	38 % "good" regrowth	Yes
Shapiro et al.	J. Am. Acad. Dermatol.	1993	Alopecia areata > 50 % hair loss	15	24 weeks + 5% minoxidil	33.3% marked regrowth	Yes
van der Steen et al	Dermatology	1991	Alopecia areata	139	> 7 months	30.2% complete 20.1% partial	Yes
Berth-Jones et al	Clin. Exp. Dermatol.	1991	Alopecia totalis	22	6 months	9.1% response	Yes

Naldi et al., 1990, assessed the efficacy of topical sensitizers for the treatment of alopecia areata in a review of 26 papers on "published clinical trials on dinitrochlorobenzene, squaric acid dibutylester, and diphencyprone [DPCP] each published between January 1977 and January 1988." The authors of the paper stated, "According to our evaluation, the published literature is of limited use in defining the role of topical immunotherapy in alopecia areata. Half the studies examined used informal methods (uncontrolled or historically controlled trials)... In general, the studies that we examined had serious drawbacks in reporting critical procedures such as assessing treatment and selecting and following up patients...In conclusion, a definite role of topical immunotherapy for alopecia areata has yet to be established and this treatment should be offered only as an experimental modality..."

In 1998, Rokhsar et al. examined the efficacy of contact sensitizers in alopecia areata in a summary review of the literature. They reported a response rate range from 9% to 85%. This range included the sum of both complete and partial responders. The weighted average response rate was 58%, similar to the response rate seen in the largest study by van der Steen et al. (1998). A relapse rate of about 50% was seen in the patients, even with continuation of treatment, suggesting that in many patients the response is temporary at best.

A tabular summary of the suggested role of immunomodulators (as gleaned from leading dermatological textbooks) for the treatment of alopecia areata and warts is presented in Table 3. Many therapeutic alternatives exist for these conditions.. The consensus is that DPCP is an experimental therapy, with a modicum of short-term efficacy. Additional well-controlled, long-term studies are needed to evaluate efficacy.

Assessment 6: There is little evidence that DPCP is effective in the long-term treatment of alopecia areata or verruca. Treatment of alopecia areata with DPCP may provide an increase in hair of variable cosmetic quality during treatment. This hair may be lost if therapy is stopped.

Table 3 - Perspectives on Treatment for Alopecia Areata and for Warts

Reference	Disease	Treatment of Choice	Other Suggested Treatments	Role of DPCP in Therapeutic Armamentarium
Andrews' Diseases of the Skin: Clinical Dermatology, ed. by Arnold et al., Eighth edition (1990) (textbook)	Alopecia Areata—patchy involvement	Intralesional injections of corticosteroid	"None of the other various therapeutic approaches are clearly superior to corticosteroids"	DPCP: not discussed
	Alopecia Areata—totalis/univer-salis	Systemic (IM) steroids should be "seriously considered".		
	Common/ Plantar Warts	Treatment of choice not identified	A, B, C, D, E, F, G, H, I, J, K (not plantar warts), L, M	DPCP: not discussed
Dermatology in General Medicine, ed. by Fitzpatrick et al., Third edition (1987) (textbook)	Alopecia Areata	Treatment of choice not identified	N (little efficacy), P, Q, R	DPCP: not discussed
	Warts	Treatment of choice not identified	A, B, C, D, E, F, G, H, I, J, K, T, U, V	DPCP: not discussed
Textbook of Dermatology, ed. by Rook et al., Fourth Edition (1986) (textbook)	Alopecia Areata	Treatment of choice not identified	O (unclear if regrowth is maintained), P (not helpful in alopecia totalis—except for eyebrows), W, X, Y, Z	DPCP: not discussed
	Warts	Treatment of choice not identified	B, C, D, L, L', E, H, I, J, T, A', B', ; avoid A,U (risk of scarring)	DPCP: not discussed
Pediatric Dermatology, ed. by Schachner and Hansen, (1988) (textbook)	Alopecia Areata	Topical corticosteroids, alone or under occlusion; Intralesional corticosteroids	O (for severe involvement, unresponsive to topical or intralesional treatment)	DPCP: as effective as DNCB (another topical sensitizer). "Here again these chemicals [DPCP] cannot be regarded as completely safe until extensive toxicologic evaluation has been completed."
	Warts	Treatment of choice not identified	A, B, C, G, K	DPCP: not discussed

A: Electrodesiccation and curettage; **B**: Cryotherapy; **C**: Salicylic Acid; **D**: Lactic Acid; **E**: Trichloroacetic/ other caustic acids; **F**: Podophyllin; **G**: laser; **H**: 5-Fluoro-uracil; **I**: Retinoids; **J**: Interferon; **K**: Cantharin; **L**: Formalin; **L'**: Glutaraldehyde; **M**: Bleomycin; **N**: Topical corticosteroids; **O**: Systemic corticosteroids; **P**: Intralesional corticosteroids; **Q**: Anthralin; **R**: PUVA (Psoralen and UV-A); **S**: Inosiplex; **T**: Bleomycin; **U**: Surgical excision; **V**: Vaccination with autogenous-wart extracts; **W**: Ultraviolet radiation; **X**: Minoxidil; **Y**: Dithranol; **Z**: Zinc sulfate; **A'**: Levamisole; **B'**: Photodynamic inactivation; **C'**: Psychological methods (hypnosis)

VI. Conclusions

Assessment 1: Although DPCP is well characterized, it degrades readily by basic hydrolysis or exposure to light. The degradation products have not been identified. DPCP used in compounding could vary significantly from DPCP used in literature studies in the level and types of impurities present; this could result in altered clinical properties and toxicities.

Assessment 2: DPCP is photo-genotoxic. Mammalian genotoxicity, chronic toxicity, reproductive toxicity, and carcinogenicity studies have not been conducted with DPCP. Thus, it is not known what the potential toxicities of DPCP are in humans or whether it is likely to be teratogenic in humans.

Assessment 3: There is limited characterization of the human safety profile. With human exposure to DPCP, adverse side effects have been reported in the literature, including erythema multiforme, eczematous dermatitis, urticaria, persistent vitiligo and post-inflammatory pigmentation changes.

Assessment 4: Many approved products are available for the treatment of verruca and alopecia areata.

Assessment 5: Since its first clinical report in 1983, DPCP has been used as an experimental treatment alternative for alopecia areata and verruca vulgaris. Evidence of its widespread use is not apparent.

Assessment 6: There is little evidence that DPCP is effective in the long-term treatment of alopecia areata or verruca. Treatment of alopecia areata with DPCP may provide an increase in hair of variable cosmetic quality during treatment. This hair may be lost if therapy is stopped.

VII. Recommendation:

Four criteria have been used to evaluate DPCP for inclusion on the bulk drug compounding list: (1) the chemical characterization of the substance; (2) the safety of the substance; (3) the historical use of the substance in pharmacy compounding; and (4) the available evidence of the substance's effectiveness or lack of effectiveness. Our evaluation of DPCP, based on a balanced assessment of each criterion in the context of the others, leads to our recommendation that it is not appropriate for DPCP to be included on the list.

The nonclinical studies conducted to date minimally evaluate the safety of diphenylcyclopropenone. The studies do not characterize the potential toxicity to internal tissues nor do they characterize the dermal toxicity from long term topical application. Conclusions about the safety of DPCP cannot be made before such studies are done.

The evidence from historical use suggests that DPCP may be useful as second or third line therapy for warts and possibly as a therapy for alopecia areata. It is our impression that DPCP has become more commonly used as a topical sensitizer than dinitrochlorobenzene (DNCB), largely because the latter compound, available for toxicologic evaluation for more than 20 years, has well-established toxicities. The notion seems to be that the known toxicities of DNCB make it less attractive than the unknown toxicities of DPCP.

If DPCP is not placed on the list of bulk drug substances for compounding, a physician/investigator could still file an investigational new drug application (IND) for use of DPCP in humans. Pursuing this route would provide important and clinically relevant information about: (1) the chemistry of DPCP (i.e., its stability, its comparative solubility in different vehicles), (2) the safety profile – pharmacology/toxicology of DPCP (i.e., safety information about long-term dermal usage), and (3) the clinical side effect profile (i.e., risk of pigmentary and eczematous reactions).

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APPENDIX SECTION C

Summary Report

Diphenylcyclopropenone

Prepared for:

Food and Drug Administration
Clinical use of bulk drug substances nominated for inclusion on the 503B Bulks List
Grant number: 2U01FD005946

Prepared by:

University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI)
University of Maryland School of Pharmacy

January 2020

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REVIEW OF NOMINATION

Diphenylcyclopropenone (DPCP; UNII code: I7G14NW5EC) was nominated for inclusion on the 503B Bulks List by the American Society of Health-System Pharmacists (ASHP) for the treatment of extensive alopecia areata via topical solution at variable strengths, usually 2%.

The reason provided for nomination to the 503B Bulks List is that there are limited topical options available for treating alopecia areata.

METHODOLOGY

Background information

The national medicine registers of 13 countries and regions were searched to establish the availability of DPCP 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 DPCP; name variations of DPCP 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(s); 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 5.1.4) and the Natural Medicines database were searched for availability of over-the-counter (OTC) products containing DPCP. 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

Two databases (PubMed and Embase) were searched including any date through July 28, 2018. The search included a combination of (diphenylcyclopropenone[TIAB] OR diphencyprone[TIAB] OR dpcp[TIAB]) AND (clinical[TIAB] OR therapy[TIAB] OR therapeutics[TIAB] OR alopecia[TIAB] OR warts[TIAB]) AND humans[MeSH Terms] AND English[lang] NOT autism. Peer-reviewed articles as well as grey literature were included in the search. Search results from each database were exported to Covidence®, merged, and sorted for removal of duplicate citations.

Study selection

Articles were not excluded on the basis of study design. Articles were considered relevant based on the identification of a clinical use of DPCP or the implementation of DPCP in clinical practice.

Articles were excluded if not in English, a clinical use was not identified, incorrect salt form, or if the study was not conducted in humans. Screening of all titles, abstracts, and full-text were conducted independently by two reviewers. All screening disagreements were reconciled by a third reviewer.

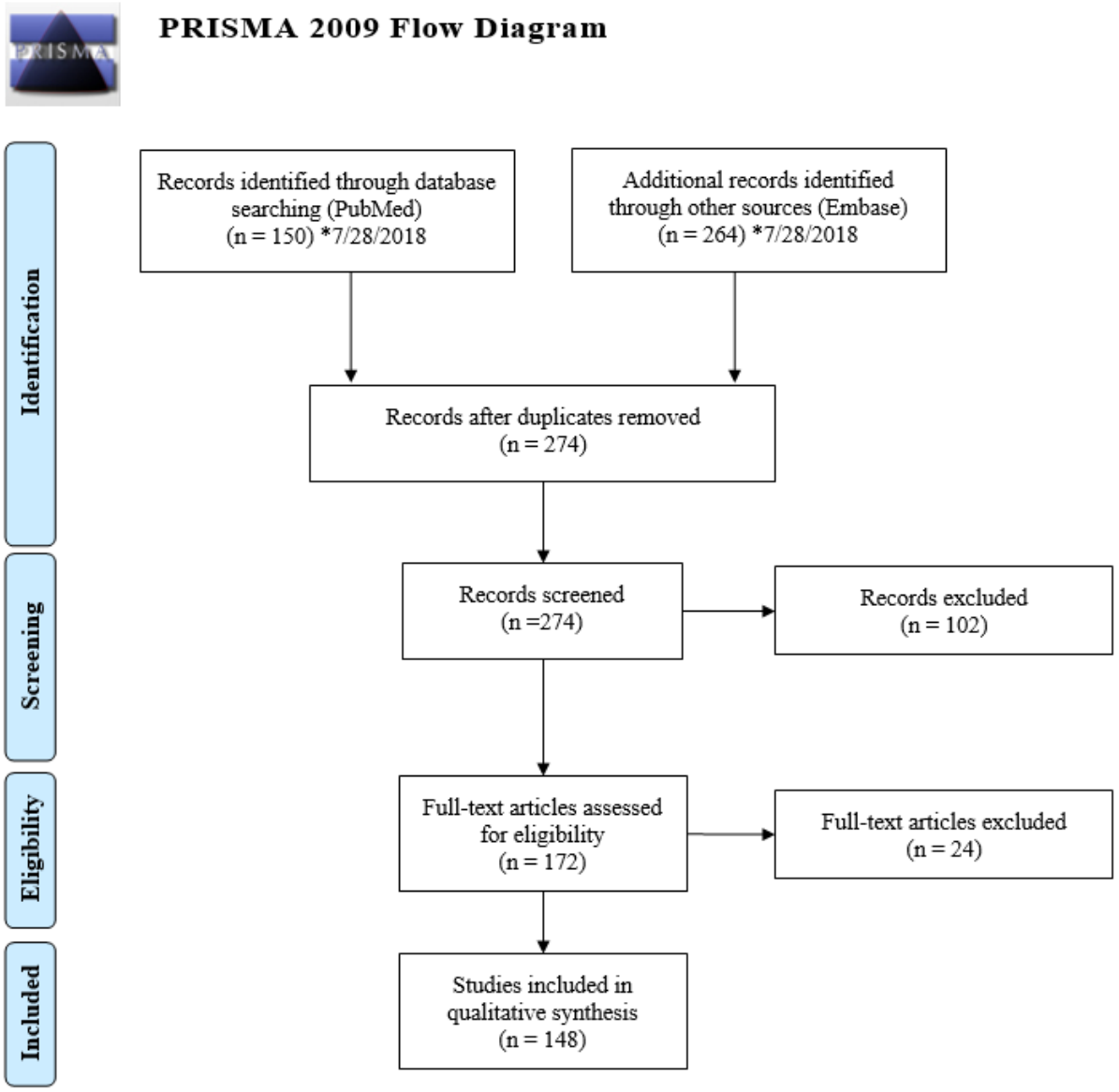
Data extraction

A standard data extraction form was used to collect study authors; article title; year published; journal title; country; indication for DPCP use; dose; strength; dosage form; ROA; frequency and duration of therapy; any combination therapy utilized; if applicable, formulation of compounded products; study design; and any discussion surrounding the use of DPCP compared to alternative therapies.

Results

Please refer to Figure 1.

Figure 1. Summary of literature screening and selection (PRISMA 2009 Flow Diagram)



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

Outreach to medical specialists and specialty organizations

Using the indication from the nomination and the results of the literature review, two (2) medical specialties that would potentially use DPCP were identified: dermatology and oncology. Semi-structured interviews were conducted with subject matter experts within these specialties. Interviews lasted from 30-75 minutes and were conducted either via telephone or in-person. Criteria for selecting subject matter experts included recommendations provided by specialty professional associations, convenient geographic location, authorship within the specialty, or referral by an interviewee. Up to nine (9) interviews were conducted per substance. Four (4) experts were contacted for interviews, of which three (3) accepted and zero (0) declined interviews. One (1) expert did not respond to requests for interview. The interviews were recorded and transcribed via ©Rev.com. QSR International's Nvivo 12 software was utilized for qualitative data analysis. The University of Maryland, Baltimore IRB and the Food & Drug Administration RIHSC reviewed the study and found it to be exempt. Subject matter experts provided their oral informed consent to participate in interviews.

Survey

General professional medical associations and specialty associations for dermatology and oncology, identified from the nomination, literature review, and interviews, were contacted to facilitate distribution of an online survey. A Google™ search was conducted to identify relevant professional associations within each specialty. Associations were included if their members are predominantly practitioners, national associations, and organizations focused on practice within the US. Organizations without practicing physicians and state or regional organizations were excluded. The association's website was searched in order 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 online survey was created using Qualtrics® software (Provo, UT). The survey link was distributed to five (5) associations. If an association had more than one (1) substance with indications relevant to that specialty, substances were combined into one (1) survey with no more than 14 substances per survey. Table 1 highlights the associations that agreed to distribute the survey link and Table 2 includes the associations that declined to participate. Additionally, single substance surveys were created and posted on the project website which was shared with survey participants.

Participation was anonymous and voluntary. The estimated time for completion was 30 minutes with a target of 50 responses per survey. The Office of Management and Budget (OMB) approved this project.

Table 1. Participating associations

Specialty	**Association**
Dermatology	American Academy of Dermatology (AAD)
	American Society for Dermatologic Surgery (ASDS)

Table 2. Associations that declined participation

Specialty	Association	Reasons for Declining
Medicine	American Medical Association (AMA)	Failed to respond
	American Osteopathic Association (AOA)	Failed to respond
Oncology	American Society of Clinical Oncology (ASCO)	Declined

CURRENT AND HISTORIC USE

Summary of background information

- DPCP is not available as an FDA-approved product.
- DPCP is not available as an OTC product in the US.
- There is no current United States Pharmacopeia (USP) monograph for DPCP.
- DPCP is not available in any of the national medical registries searched.

Table 3. Currently approved products – US

No approved products in the US

Table 4. Currently approved products – select non-US countries and regions

No approved products in select non-US countries and regions

Summary of literature review

- Total number of studies included: 148 (63 descriptive, 53 experimental, and 32 observational).
- Most of the studies were from the UK (32), followed by Korea (20).
- The most prevalent indication in the US and non-US studies was alopecia areata, followed by warts.
- Application of DPCP ranged from every four weeks to daily.
- Compounded DPCP products in the nominated dosage form was identified from US and non-US studies for alopecia areata and warts.

Table 5. Types of studies

Types of Studies	Number of Studies
Descriptive[1–63]	63
Experimental[64–116]	53
Observational[117–148]	32

Table 6. Number of studies by country

Country	Number of Studies
Australia[4,5,7,9,27,52,68–70,87,97,99]	12
Bosnia[30]	1
Brazil[16]	1
Canada[35,48,49,59,101,134,138,142]	8
China[77,124,128]	3
Denmark[88,144]	2
Egypt[2,72,82]	3
Germany[11,12,54,56,79,81,108,127]	8
Greece[17,80,103,109]	4
Hungary[105]	1
India[19,20,71,102,107,140]	6
Iran[40,64,65,73,76]	5
Italy[42,43,60,67,75,110,137]	7
Japan[14,84,145]	3
Korea[28,31,34,62,66,83,85,86,93,95,104,118,119,122,129–131,133,135,146]	20
Lebanon[8]	1
Poland[112]	1
Saudi Arabia[1]	1
Spain[6]	1
Switzerland[46,132]	2
Thailand[3,106,136]	3
The Netherlands[32,41,55,96,100,111,139,141]	8
Turkey[33,143]	2
United Arab Emirates[74]	1
UK[10,13,15,21,22,24,26,37–39,44,45,50,53,57,61,63,78,90–92,98,113–115,120,121,123,125,126,147,148]	32

US[18,23,25,29,36,47,51,58,89,94,116,117]	12
	Total US: 12 Total non-US countries: 136

Table 7. Number of studies by combinations

No combination products were nominated

Table 8. Dosage by indication – US

Indication	Dose	Concentration	Dosage Form	ROA	Duration of Treatment
Alopecia areata[23,25,29,36,47,51,117]	Apply twice weekly-every 2 weeks	0.0001%-7%	Solution	Topical	3 months-15 years
Warts[23,36,58,94,116]	Apply daily-every 3 weeks	0.01%-2%	Solution	Topical	0.8-8.6 months
	Apply weekly	0.04%-0.4%	Ointment		10 weeks
Melanoma[18,23,36]	Apply twice weekly	–	–	Topical	14 weeks
Measure of immune competence in HIV positive patients[89]	–	0.05%-0.4%	–	Topical	Once

Abbreviations: "–", not mentioned; ROA, route of administration.

Table 9. Dosage by indication – non-US countries

Indication	Dose	Concentration	Dosage Form	ROA	Duration of Treatment
Alopecia areata[1,2,8,11,12,15,17,19,22,24,26,28,30,32,33,35,37-40,43,46,48,49,53,54,57,60,61,63,64,67,71-75,77-82,84,85,90-93,98,100-103,105-112,114,118-122,124-129,132-137,139-143,145,147,148]	Apply every 1-4 weeks	0.0000001%-5%	Solution	Topical	1 week-5 years
Warts[9,10,13,34,42,45,55-57,61,62,65,66,87,88,95,96,104,115,130,131,138,144,146,147]	Apply every 1-4 weeks	0.0001%-6%	Solution	Topical	Up to 10 weeks
	Apply nightly-every 3 weeks	0.01%-5%	Ointment		Up to 18 months
Melanoma[4,5,7,14,16,21,27,41,44,50,52,59,61,68-70,97,99,123,147]	Apply every 1-2 weeks	0.1%-2%	Solution	Topical	1-60 months
		0.00001%-10%	Cream		
Molluscum contagiosum[3,31,83,86]	Apply every 1-2 weeks	0.0001%-2%	Solution	Topical	6-20 weeks
Vitiligo[20,76]	Apply weekly	0.0001%-2%	Solution	Topical	6-10 months
Satoyoshi syndrome[6]	Apply weekly	–	–	Topical	–
Sensitization pretransplant[113]	–	0.001%-0.1%	–	Topical	–

Abbreviations: "–", not mentioned; ROA, route of administration.

Table 10. Compounded products – US

Indication	Publication Year	Compounding Method	Dosage Form	Final Strength
Alopecia areata[47,51]	1998, 2015	• Dissolve in acetone	Solution	2%
Warts[58,94]	1988, 2015	• Dissolve in acetone	Solution	1%-2%
Measure of immune competence in HIV positive patients[89]	2006	• Diphenylcyclopropenone • Polysorbate 80, USP/NF • Isopropyl myristate, USP/NF	–	0.05%-0.4%

Abbreviation: "– ", not mentioned.

Table 11. Compounded products – non-US countries

Indication	Compounding Method	Dosage Form	Final Strength
Alopecia areata[1,8,15,17,26,38,40,48,57,60,64,67,72,74,75,78-82,84,85,90-93,98,109,114,124,125,143]	• Dissolve in acetone	Solution	0.000001%-5%
	• 9:1 mixture of methylated spirit 95% and propylene glycol		1%
Warts[65,66,87,88,115,144,146]	• Dissolve in acetone	Solution	0.001%-6%
	• In petrolatum	Ointment	0.01%-5%
	• Diphenylcyclopropenone • Salicylic acid • White soft paraffin		0.1%
Melanoma[5,16,21,59,69,70]	• Dissolve in acetone	Solution	2%
	• In aqueous cream	Cream	0.00001%-10%
	• In Glaxal-based cream		0.01%-0.1%
Mulluscum contagiosum[31,83,86]	• Dissolve in acetone	Solution	0.0001%-1%
Vitiligo[76]	• Dissolve in acetone	Solution	0.001%-2%

Summary of focus groups/interviews of medical experts and specialty organizations

Three (3) interviews were conducted. One (1) medical expert with a Doctor of Medicine (MD) specializing in oncology failed to respond to interview requests.

Table 12. Overview of interviewees

Interviewee	Level of Training	Specialty	Current Practice Setting	Experience with DPCP	Interview Summary Response
DER_01	MD	Dermatology	Academic medical institution Faculty at a School of Medicine	Yes	• Does not use it as much anymore due to change in practice • Not first line for anything
DER_02	MD	Dermatology Dermatology/Immunology	Independent consultant	No	• Feels "fairly familiar" with it • Does not feel there is strong evidence for use in alopecia areata, warts, or viral infections
NAT_01	ND	None	Private practice	No	• Does not purposefully use DPCP

Abbreviations: MD, Doctor of Medicine; ND, Naturopathic Doctor.

Use of DPCP

- One (1) interviewee reported being "fairly familiar" with it, despite not being readily available when interviewee saw patients.
    - States that the information to support use are predominantly individual case reports; has not been well-studied.
- One (1) interviewee reported not purposefully using DPCP at all.
- Alopecia areata
    - Two (2) interviewees discussed alopecia areata, but neither consider DMPS to be first line. Both mentioned injecting steroids into the site as one of the starting therapies in alopecia areata, but both state they are not hair experts.
    - One (1) interviewee stated that the idea is to "let the patient develop an allergic contact dermatitis at the site, then you're going to distract the immune system and distract the T cells and it will allow their hair to regrow."
        - Current interest in JAK inhibitors, but nothing is approved for alopecia areata, just "inflammatory skin diseases."
    - One (1) interviewee commented that use might come down to patient preference (contact dermatitis versus injection).
    - One (1) interviewee said, "most cases that are treated promptly are responsive to treatment. And treatment only persists as long as it takes for regrowth to occur."

- Warts and molluscum
    - Two (2) interviewees discussed using DPCP for warts. One (1) interviewee stated that the first line treatment is freezing with liquid nitrogen and paring with a blade. This is to "create some kind of local trauma to elicit an immune response."
    - Two (2) interviewees stated that the idea behind using DPCP for this indication is to create an immune reaction.
        - One (1) interviewee noted the body might not create the same immune response since warts are in the epithelium. There are also concerns with itchy contact dermatitis, patient scratching, and autoinoculation of the warts.
        - Another interviewee commented that "if you can freeze even one wart badly enough, or do something with it, or treat it with DPCP, or whatever, to the fact that it goes away, often all of it will go away at the same time, because think if the immune system wakes up and just wipes them all out at the same time."
    - One (1) interviewee said that when using DPCP for treating warts, they see the patient every three or four weeks to repeat the treatment. If it does not work after two or three times, they move to something else.
- Metastatic melanoma
    - One (1) interviewee stated has not used DPCP for this indication, but that the idea is to stimulate the immune system to attack the melanoma. Did not think this is a common indication; would be done for comfort or as part of many methods.

Comparison with other topical irritants

- One (1) interviewee said that they think that all are comparable in use.

Use of "office stock"

- One (1) interviewee commented that sensitization with a high concentration typically occurs in the office. Once sensitized, the dosage form for maintenance dosing does not matter.
- Another interviewee stated they would not want patients to self-administer in order to avoid user error. Would be useful to stock if something that the provider does regularly so when the patient is there, they can get treatment.

Use in pediatric patients

- One (1) interviewee expressed concern about administering DPCP to children, "There's a higher standard that goes into clinical trial development. You have to have data to say that something has a benefit before you're allowed to proceed into dosing children."

Potential concerns with using this product

- One (1) interviewee commented that you are essentially inducing allergic contact dermatitis, and there is a secondary risk of infection.
    - Must consider individual patient response based on how "twitchy" the immune system is.
- One (1) interviewee has no concerns about inadvertently sensitizing anyone since there are other compounds that are more prevalent in the environment and more likely to cause issues (such as nickel and chromates).

Emergency use

- One (1) interviewee stated, "N-O. It is not an emergency ever."

Summary of survey results

Table 13. Characteristics of survey respondents [5 people responded to survey]

Board Certification	MD	No Response
Dermatology	2	0
No Response	0	3

Abbreviation: MD, Doctor of Medicine.

Table 14. Types of products used, prescribed, or recommended

Types of Products	Respondents, n (N=2[a])
Compounded	1
FDA-approved	1
Over-the-counter	0
Dietary	0
Unsure	0
No response	1

[a]Out of five (5) respondents, two (2) reported using, prescribing, or recommending multiple types of DPCP product.

Table 15. Compounded use of DPCP in practice

No survey respondents provided this information

Table 16. Indications for which DPCP is considered a standard therapy

No survey respondents provided this information

Table 17. Reasons for using compounded product instead of the FDA-approved products

No survey respondents provided this information

Table 18. Change in frequency of compounded DPCP usage over the past 5 years

No survey respondents provided this information

Table 19. Do you stock non-patient specific compounded DPCP in your practice?

No survey respondents provided this information

Table 20. Questions related to stocking non-patient specific compounded DPCP

No survey respondents provided this information

CONCLUSION

DPCP (UNII code: I7G14NW5EC) was nominated for inclusion on the 503B Bulks List to treat extensive alopecia areata as a topical solution. DPCP is not currently available in any of the national medical registries searched.

From the literature review conducted, the most common indications in US and non-US countries were alopecia areata and warts. Compounded DPCP products in the nominated dosage form was identified from both the US and non-US studies.

From the interviews, one (1) interviewee reported experience with DPCP and one reported being "fairly familiar" with it, despite not having been readily available when the interviewee previously saw patients. Neither of the interviewees who specialized in dermatology consider themselves "hair experts," where use of DPCP for alopecia areata would be most common, however, they both stated that it is used, just not typically first line. Since sensitization with DPCP typically occurs in the office at a high concentration stocking bulk DPCP in the office may be useful if the provider treats alopecia areata regularly. They also described DPCP use for warts and molluscum (not first line) and uncommonly metastatic melanoma.

From the survey responses, two (2) out of five (5) respondents used DPCP and one (1) respondent reported using both compounded and FDA-approved DPCP products.

APPENDICES

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Appendix 2. Transcripts from focus groups/interviews

INTERVIEW_DER_01

Interviewer 1: If it any time during the interview, you wish to discontinue the use of the recorder, or the interview itself, please feel free to let me know. I do not anticipate any foreseeable risk or discomfort to arise from your participation in this session, however there is the potential for loss of privacy and confidentiality. All of your responses are confidential, and we ask that you do not discuss responses to this interview outside of this room. Your name will not be documented in the final report submitted to the FDA for review. If you have any additional questions or concerns after the end of the session, you can send me an email, and I can provide you with your rights as a research subject by contacting our HRPO office. Do you have any questions or concerns before we begin?

DER_01: Nope.

Interviewer 1: So like I mentioned, the substance that we are primarily focused on is DPCP, or diphenylcyclopropenone. We did conduct a literature review, and found that the primary indication, there are some additional indications, but I was hoping we could talk about what the primary one seems to be, in alopecia areata. A lot of the studies that we found were not based in the United States; most of them were overseas. I think there was actually some reports about it, and I'm blanking on the name of it, but in the U.K., it's part of their dermatologic guidelines for alopecia areata. Could you talk a little bit about your experience with DPCP? Is this a substance that you use in your current practice setting?

DER_01: It is a substance I have used in my current practice setting. My practice has evolved over time, so I can't personally use it anymore, because now my practice is more restricted to treatment of skin cancer. But earlier, I did use it. In fact, I think we even reported a case of an adverse event from DPCP, not related to purity, but just sort of a very vigorous immune reaction. I think we reported it in JAAD a number of years ago, again, for alopecia areata, as you indicated.

DER_01: So I think when I did use it, and I think when people do use it, it is intended for treatment of alopecia areata, most commonly, and it's usually something that I wouldn't say is always first line. But alopecia areata can be a profoundly disfiguring and alarming condition for people, because it's not the same as pattern baldness, which seems kind of normal, but the peoples' hair is kind of falling out in chunks, and sort of in odd places, they look diseased, they look disfigured, they might be very young when this happens, and it impacts their self-esteem and ability to interact with other people, to feel confident about themselves, there's also a sense of foreboding, which is if you wake up and suddenly all the hair on one side of your head is gone, what's going to happen next. So even though it sounds like while this is not a cancerous condition, and it's fundamentally a benign condition, and then if don't believe it leads to serious health issues of some type, it is something that people are very worried about.

DER_01: So then you try a variety of things when you get alopecia areata; among the first things that you do is you inject steroids, so that steroid injection's into the site to try to get hair follicles to wake up. And then if that doesn't work, then there's a variety of other treatments, [inaudible 00:03:33] of any sort of topical immunotherapies like DPCP, or DNCB. And they can be helpful in kind of waking up the hair follicle and restarting the hair cycle. So I think it's definitely something that's been in the armamentarium for a

while, it's described in clinical use. I agree with you, there are not a lot of, quite any, I don't know if there are any randomized controlled trials on large cohorts, but that's to be expected, because the use of DPCP if it's not a first line drug that you're doing in a lot of people, it's difficult to enroll for a study, just like rare adverse events. It's hard to have a prospective trial with something that happens quite infrequently. And also because, I think historically, even though dermatology would perceive alopecia areata as a serious, disfiguring- you'd be amazed how upset people are when they have this, but they really are, and it's really ruining their lives.

DER_01: While we perceive it that way, you can imagine this is not the sort of thing where the NIH is going to set aside a large amount of money and say, "Well, we're not going to fund breast cancer research, but instead we're going to focus our money this year on alopecia areata." So as a consequence, in the absence of large amounts of money like that, that are funded through national agencies, how are you going to fund a large study? Who's going to pay for it? A large pharmaceutical company isn't going to pay for it, because this drug isn't under patent protection; in fact, it's more of a chemical, than a drug. So I think that lack of a lot of systematic research and trials is not indicative of the fact that the [inaudible 00:05:36] it useful, but just is a manifestation of the reality that certain sorts of effects, based on the infrequency and the limitation in research funding, are very difficult to study systematically.

Interviewer 1: So in terms of treatment of alopecia areata, you had mentioned that the steroid injection would kind of be your primary go-to. So where in the line of treatment options would this particular substance fall?

DER_01: That's a good question. I don't know if I can answer that with the specificity that maybe you would like, because I think that would vary. It would vary from person to person; in terms of both, in terms of practitioner to practitioner, and also in terms of patient to patient. Because once you've done the easy things, and if they haven't worked, then you present a number of options to both yourself, and possibly to the patient. And you go over the pros and cons. And then, some practitioners will have greater luck with, or feel like some things are better in the absence of really, really good data, and then others will- so, I think very few people will say, "Well, that's a terrible thing to admit, that you use that for alopecia areata." But exactly which order people would use it in, I think to some extent, that would be a matter of preference.

Interviewer 1: So, I guess it's kind of one of those like you kind of weigh each patient individually to kind of see what might be the best option, depending on what you've tried, and kind of things like that.

DER_01: Right. And it could be the whole spectrum. It could be some patients that say, "Well, that didn't work on me so I'm just going to stop" and other patients could be like, "Well, this, and then that," and the kind of adverse event that patients are okay with, like if they don't want something that's going to make their scalp itchy and red, well, then, maybe this wouldn't be right for them. Or if they said, "Listen, I'm willing to try anything, but I don't want an injection," well then this might be better. That sort of thing.

Interviewer 1: And I guess kind of my understanding from what we've read throughout the course of the literature, is it seems that 2% seems to be the common strength that you would use to, I guess, sensitize the scalp, and then depending on the reaction, you would do various

strengths of the substance to elicit the reaction toward, like a mild dermatitis, almost. Is that correct?

DER_01: That's absolutely true.

Interviewer 1: And it seemed like, it may again just be like a very specific type of thing, it seemed like the treatment strength options varied from anywhere from like .0001%, all the way up to, I think we have some that show that they even went up to like 5% or 7%. Is that mostly just, it just depends on what the patient reacts to, that will determine what type of strength you'll need for treatment?

DER_01: I think that's exactly right. I think the preference is to use the lowest strength that would be successful in eliciting a dermatitis sufficient to cause hair regrowth.

Interviewer 1: When you did use this substance, how frequently would you say that you used this particular substance?

DER_01: I apologize. I'm eating at the same time. Relatively infrequently, I would say, and that is also because even when I was doing more general dermatology, I wasn't a hair person, per se. So the amount of hair, and then hair problems, and then alopecia areata, are going to be seen preferentially by general dermatologists rather than dermatopathologists and dermatologic surgeons or whatever, and within that subset, they're going to be seeing, and this has evolved, I think even in the last 20 years or so, increasingly there's more subspecialization dermatology, so I think a lot of people with alopecia areata are eventually, especially with the resistant alopecia areata, which is what I think is a very common outcome, but also probably the best indication for DPCP, will also now present to somebody who has a special interest in hair disorders. But yes, I wouldn't say even a hair person would be necessarily doing this five times a day. But they might be doing it a few times a month, where somebody who's not a hair person might be doing it a few times a year, or even less.

Interviewer 1: How frequent is alopecia areata? Is it a relatively uncommon disease?

DER_01: It is a very common disease. It is such a common disease that I've had it personally.

Interviewer 1: Okay. I didn't realize that.

DER_01: It had nothing to do with this. I used DPCP 20 years ago, and then three years ago, I had alopecia areata. I woke up one day, and I noticed, my beard is much more full on one side than the other, and I was like, "Did I just shave it better on one side?" And I had one dermatologist come look at it, and then she looked at my head, and she said, "Oh, you also have a bald patch here on your head." And I was like, "I have what?" So it was very alarming, and actually I have some personal experience, and I always thought like, "Well, alopecia areata, another kooky person is worried that they're missing three hairs." But I was like, "I'm only like 40. Why do I have [inaudible 00:11:47] on my head?" It was very alarming, and it was kind of embarrassing to have half a beard.

DER_01: So I actually did get the steroid injections, and they're excruciating, and I got them every two weeks for about a year. And finally I got some regrowth. But having someone stick 15 needles into your face every two weeks is not a fun thing. It really was very distressing. And I'm not a particularly vain person [inaudible 00:12:14]. Even though I do cosmetic dermatology for a living, I've never had a cosmetic procedure myself. But it was very distressing, and it's quite common. I don't know exactly what the percentage is, but I

would put it on the order of millions of Americans have had it. I don't know how many millions, but millions.

Interviewer 1: You said that you were treated for about a year. So is it something that you stop treatment once regrowth starts, or is it something that you have to continue treatment indefinitely?

DER_01: I think usually once you get regrowth, you can stop treatment, and someone might have a relapse in a few years again, and require another episode of treatment. But I think the most common outcome is, you get it, you get some treatment or series of treatments, and you get partial or complete resolution. That's the most common. Now there are, of course, unusual cases, even of children who get alopecia totalis, where they don't have a single hair on their entire bodies, and it stays that way forever. But I'd say most cases that are treated promptly are responsive to treatment. And treatment only persists as long as it takes for regrowth to occur.

Interviewer 1: In terms of DPCP, what would be the frequency in which somebody would be treated? Because one of the things that we kind of started to notice in the literature was, it seemed like not many patients would do the treatment at their house. They would actually go to, I guess, the physician's office to have the treatment applied, and then they would leave. So I guess, how frequently would the patient have to go into the office, or would this be something that you would give the patient to do at home?

DER_01: Not the latter. I think this is something we would want to do in the office, at least that's how I've always done it. With regard to frequency, you have to really think back; I can't really remember all the frequencies, but it's not something you're doing on a daily basis, obviously. And it's obviously not something you're going to keep doing for years, because either it's going to work, or it's not going to work. So I don't know how to answer that super well, because I don't want to generalize. Again, it's somewhat distant, so I can't really- I don't remember it well.

Interviewer 1: So in terms of the patient population-

DER_01: You wouldn't want to give it to patients, because it's hard to do, it's hard to see where the hell you're putting it, how much you're putting, and you just don't want to have the patient just think, "Oh, maybe I should've just put it in a cup or drank it, or something like that." You just don't know what people are going to do if you give them stuff, and it's not really something that has like a package insert and clear instructions, and it's meant for home application.

Interviewer 1: That's some of the other piece of what we're trying to uncover is the first step is, what's the clinical use? Is there a clinical need for the particular substance? And then the second piece of it is, well, if there's a clinical need, what's the reasoning why an outsourcing facility would be the one that when you can make it from a bulk substance. So a compounding pharmacy, for example, that they get a prescription for the patient, they dispense it to the patient, or the physician sends the prescription to the pharmacy, the pharmacy sends the drug to the physician's office, so the outsourcing facility doesn't have to have that. So the outsourcing facility can make a bunch of the product up, they can send it to the physician's office for them to keep it, and then as patients come in, they can administer it to their patients.

Interviewer 1: So the other piece of this would be, is there a particular reason why, as a practitioner, you would want to stock it in your office, versus getting those patient-specific prescriptions?

DER_01: That's a good question. I think it depends a lot on what sort of practice people have. My sense is somebody who is interested in hair, like in our practice, we have a large-ish practice, an academic practice of about 20 general dermatologists, so we have two people who have a specific interest in hair. They don't do hair full-time, but they do maybe hair half-time each. So, for those people, and if you want to extrapolate, a significant percentage of dermatologists, maybe single digits, but that's still hundreds of people, maybe a thousand people, for those doctors, I think it would be useful to stock it, because that's what they do for a living, so it's kind of problematic, if somebody waits two months to get an appointment for hair, and then they're there, and then it's like, well, gee, we don't really have it today, but we'll make it [inaudible 00:17:24] come back in a couple of months. Or, you've had it the last two times, but now, we've run out because we didn't get a new prescription for you, so now I need to get another prescription maybe each time you come here to apply it we have to call in another prescription for you, because if we don't, then where are we going to maintain your bottle, and then also, of course, the added expense. Because there's no specific reason , this is not some sort of super sterile compound, where you're going to need to like open a vial, and you have to apply it within ten seconds before it kind of evaporates or does something bad.

DER_01: So, you have the good fortune of having something relatively affordable for patients, which is cost-effective, and now if you, many, many named prescriptions, obviously, many cases it will no longer be accessible by many patients because of cost and convenience.

DER_01: So I would say, do I need to personally, in my [inaudible 00:18:28] to have, would it make any difference to me? Probably not, because if I need it, I'd need it so rarely that probably I wouldn't even do it, I'd probably refer to somebody who does it. But for people who are seeing a number of hair patients, if this is a modality that they find useful, it would be nice for them to have it.

Interviewer 1: So there was a couple other indications that we had found for DPCP, and one of them was for skin cancer and metastatic melanoma. Would this be a substance that, would kind of cross the list of potential treatments for either one of those two?

DER_01: [inaudible 00:19:08] melanoma, and what's the other indication you mentioned?

Interviewer 1: It just said a generic skin cancer. It didn't really say too much detail about it. It was just skin cancer, and then there were a couple articles that specifically mention metastatic melanoma.

DER_01: I'm assuming for metastatic melanoma, it's kind of like a simplified form of what's currently in vogue, but has been done for many years in different ways, it's some sort of localized immunotherapy. So it's kind of almost like a topical vaccine. The idea, I think, is, with many things like that, like we've done some work with various lasers and dyes, for instance, where we find that a nodule of metastatic melanoma, once it's dead, [inaudible 00:20:00] the skin surface of someone's leg. I mean, you can cut it out, but they still have melanoma all over their body, so that's not really solving their problem.

DER_01: Another thing you can do is you can try to get the body's immune system to pay attention to that nodule, and the theory is, if you can somehow do that, then that attention can generalize to the rest of the body, and either that lung nodule might go away, too, or at least the rate of progression might be mitigated by this hyper-stimulated immune system. So I'm assuming that's the indication. I haven't used it for that, personally, but like I said, I've used other things, substances like (endotheline green?) and various lasers to zap nodules of melanoma, to elicit the same sort of response.

DER_01: So the same thing would be [inaudible 00:20:51], you're trying to get a dermatitis going there, and basically trying to recruit a variety of new modulators in the area and help them notice the melanoma cells, which maybe they can mitigate the spread of. So again, I don't think this would be something that the average dermatologist would be doing very often, and it's a much less common indication than for hair, as you indicated. And it could be something for comfort, or for one of the many methods to try to mitigate the spread of a potentially fatal disease.

Interviewer 1: So potentially, but maybe not that frequent, as much as the alopecia areata?

DER_01: It's not a bad thing to have, because, again, for somebody who has a disease of that severity, we would need to, let me see if I can wax poetic for a while, these sort of things are nice to have, because sometimes the best thing you can do is sort of give people hope and a little bit of time. And it might sound like, wow, that's not very evidence-based, but if that's all you can give them, you want to give it to them.

Interviewer 1: And then the last piece that we wanted to ask you about was, in terms of, and I assume that, kind of just based on the mechanism, that it would probably be along those same lines, just for general warts. I guess, would it make sense to, or would it be something that you would use to treat warts?

DER_01: I think wart usage would be, I would say I'd probably it higher in frequency than the melanoma usage. I've heard of the wart usage much more than I've heard of the melanoma usage. Warts are the bane of every dermatologist's existence, because they're really no- they’re ubiquitous, and if alopecia areata is common, warts are even more common. And while most warts respond to, the first line treatment for treatment of warts is freezing with liquid nitrogen and paring with a blade. You're going to pare off the skin which is infiltrated with human papillomavirus, and you see the little black dot, which is the thrombosed vessel at the base of the wart, you kind of pare down almost to that point, and then you freeze it. And by freezing it, basically what you're doing is trying to create a little ice ball, which causes the cells that contain the wart virus to rupture and go away.

DER_01: But, freezing is not a specific treatment. That's the biggest problem with warts. You don't have any specific treatment for warts. So the entire management of warts is predicated on the same thing that I was explaining earlier with melanomas. You're basically trying to create some kind of local trauma to elicit an immune response. So it's non-specific local trauma, designed to elicit a specific immune response to make the wart go away, kind of like with the melanoma example, if someone has warts on their fingers and toes and whatever, if you can freeze even one wart badly enough, or do something with it, or treat it with DPCP, or whatever, so the fact that it goes away, often all of it will go away at the same time, because think if the immune system wakes up and just wipes them all out at the same time.

DER_01: So you're basically just trying to find some way to wake up the immune system. You kind of freeze the wart, pick the wart, scrape the wart, do whatever you can possibly do. People have even tried hypnosis, and it works for some people, [inaudible 00:24:44] because they're pretty convinced that wart's going to go away, and it does. But in that way, then DPCP will be doing the same thing. It will be basically creating a local dermatitis, which will be a form of immuno[inaudible 00:25:02] that would possibly make a wart go away. That's pretty important, I would say, because there are a lot of resistant warts. We do all kinds of odd things in them: we inject bleomycin in them, we inject candida antigen in them, we even give people the vaccine that was developed for young girls for HPV, but it's a different serotype because there might be cross-reactivity between those HPV types, which are like 1831 and 35 for the genital, that's versus the whatever, 2 and 4 that are in warts. So that happens all the time, that the first line treatment for warts doesn't work, and you're trying to do everything and the kitchen sink, because every time someone, like, picks up a fork, their hand hurts, and they feel embarrassed to shake hands at a meeting, and it's kind of driving them nuts.

Interviewer 1: Would the dosing strategy be similar for the warts as for the alopecia? Or would it be more of kind of a one-time dose to see how it responds?

DER_01: I think for warts, it's usually, we see the patient back every three or four weeks, and you kind of repeat the treatment. We usually give it two or three times, at least, and give them the same treatment, to see if you can make it work. And if you can't after two or three times, then it's off to something else.

Interviewer 1: So those were all of the indications that we had found in our literature searching. Are there any indications for DPCP that we missed, that might be relevant, or helpful as we're kind of compiling all of this information?

DER_01: Not that I know of, but again, there certainly could be, but not that I know of.

Interviewer 1: So you would say those might be the more predominant ones that we would run into, the alopecia and the warts would be the most frequent uses for the substance?

DER_01: I would probably say that's true, yes, ma'am.

Interviewer 1: I think you have answered all of the other questions in some of the other conversations that we had. And then, I think you had mentioned this when we first started talking, so there's the DPCP, the DNCB, and then the SADBE. Are you familiar with the SADBE substance?

DER_01: Squaric acid?

Interviewer 1: Okay. So that's actually one that we're also looking into. We don't have as much information because that was a substance that we just received a couple weeks ago. But I guess as we're looking into it, could you maybe provide any insights or indications for that particular substance, as well, or any historical-

DER_01: I pretty much think of them in the same category, I think of DPCP, DNCB, and squaric acid as three topical sensitizers for alopecia areata. You can kind of try them, pick one you like, I don't mean like, like as in "like," but you know, to pick one to begin with, then if that didn't work, you could try a different one. So I kind of think of them with alopecia areata as just, they're not necessarily highly related in a molecular sense, but for

indications, and route of use, and [inaudible 00:28:39] and frequency of use, I think they'd be largely comparable.

INTERVIEW_DER_02

Interviewer 1.: So I have just my brief, standard consent that I have to read through for you just in regards to you talking with us today. So thank you for your participation today. My name's Ashlee Mattingly. I'm an assistant professor at the University of Maryland School of Pharmacy. I'm conducting a research study regarding the use of bulk drug substances and compounding. I hope to determine how diphenylcyclopropenone is used in your practice setting. Your participation is voluntary. While there's not direct benefit to you as a participant, the information gathered in this session will assist the FDA in its development of a list of bulk drug substances that outsourcing facilities can use in compounding under section 503B of the Food, Drug, and Cosmetic Act.

Interviewer 1.: I think we scheduled an hour for this particular conversation. If at any time you need to stop or take a break, please let me know. You may also withdraw your participation at any time without consequence. If at any time during the interview you wish to discontinue the use of the recorder or the interview itself, please feel free to let me know. I do not anticipate any foreseeable risk or discomfort to arise from your participation in this session. However, there is the potential for loss of privacy and confidentiality. All of your responses are confidential and we ask that you do not discuss responses outside of this conversation, and your name will not be documented in the final report that we submit to the FDA regarding the use of this particular substance. If you-

DER_02: Okay.

Interviewer 1.: ... if any questions, I can send you our email, and then also the phone number and email for our HRPO. Are you okay if we go ahead and get started?

DER_02: I am.

Interviewer 1.: Okay. So the reason that we were going to talk with you today was because one of the substances that we have is diphenylcyclopropenone, which we have identified has the majority of its uses for dermatologic reasons. So could you just give me a brief overview of what your current level of training is?

DER_02: Certainly. So ... It's a good idea. I'm a pharmacist in my first life and a physician trained at the University of [redacted] and I'm a dermatologist, board-certified by the American Academy of Dermatology. After my residency, I completed additional training in dermatology/immunology/lab immunology, which is DILI, and I have special certification qualification from the American Board of Dermatology, not only for dermatology, but in the dermatology/immunology subspecialty within dermatology. I spent the first half of my career in full-time academic medicine. I was full-time faculty at University of [redacted], [redacted] University, [redacted] University, and then had spent a substantive amount of time since 2000 in pharmaceutical drug development, predominantly working on the development side of the house with new chemical entities. And currently, I'm a consultant and I'm licensed to practice medicine in the state of [redacted].

Interviewer 1.: Okay. Wow. Quite the background. So the drug that we have, again, is the diphenylcyclopropenone. And, I guess, how familiar are you with this particular substance?

DER_02: I am fairly familiar with it, but I am not currently using that product, and I actually did not use it when I was seeing patients, again, because of the fact it wasn't readily available. The data that support its uses, I think ... under the guidelines of care, if you were looking at what level of data do we have, it's predominantly individual case reports for some [inaudible 00:03:58]. It's not been well-studied to document it to be able to be efficacious in what it's been advocated for.

Interviewer 1.: Okay. So I guess, briefly, so we did a brief systematic review to see what is out there that's been published. And like you mentioned, a lot of it is kind of like case series, case reports, and things like that about the particular use. So I just wanted to briefly read to you the different indications so that we can talk through, or you can talk us through, why or why you would not recommend the use for this particular substance in this particular indication.

Interviewer 1.: So we have alopecia, different and various types of warts, verruca plana. I'm probably going to butcher some of these names. Generalized molluscum contagiosum in both HIV and non-HIV infected patients, some benign dermatoses, skin cancer, metastatic melanoma, multiple squamous carcinoma, eccrine porocarcinomas, vitiligo, depigmentation, Satoyoshi syndrome, and then pre-transplant sensitization, and as a measure of immune competence.

Interviewer 1.: I think from what we've found, I think alopecia and then various types of warts were some of the most common indications that we encountered. So, I guess, could you talk us through how you would normally treat these conditions and maybe why diphenylcyclopropenone would not be high on your list for treatment?

DER_02: Right. So just as a reminder, there's lots of different types of alopecia. There's scarring alopecia and non-scarring. Alopecia areata is the one where diphenylcyclopropenone has been used, and it's an autoimmune disorder in which the activated T cells are targeting the cells involved with the hair follicle. And that autoimmune attack leads to loss of hair in very round patches, and you can make the differential diagnosis fairly easily by plucking or pulling gently around the edges of the hair, and the hairs are loose and they'll come out. And it can be localized, which it often will wax and wane and people will do fairly well. But they can get an extensive disease which can either be totalis, in which they will lose all of their hair, or universalis, where they lose the hair not on their scalp, but on their body and their eyebrows, their eyelashes. And that can be fairly devastating.

DER_02: There's a ... strong autoimmune component to this. It does tend to run with some other autoimmune diseases, so there's some HLA haplotypes associated. You typically can look for whether people have autoimmune thyroid disease as well, but not everybody does. It's often just ... And that's where this drug is used. And the idea here is if you can sensitize with this diphenylcyclopropenone and let the patient develop an allergic contact dermatitis at the site, then you're going to distract the immune system and distract the T cells and it will allow their hair to regrow. Now this doesn't work for any of the other alopecias. There's scarring alopecia like in lupus or some other scarring folliculitity and there's some other non-scarring alopecias. The most common alopecia is general

androgenetic or female/male pattern alopecia, which is one of those conditions associated with your genetics and start getting progressive thinning, and women can also have preexisting thinning. But this drug doesn't work for them, it's really the alopecia areata subgroup.

DER_02: So alopecia areata is classically treated with potent topical steroids. Sometimes people will use intralesional steroids. The most exciting thing that's happening right now in this family of disorders is actually the use of the JAK inhibitors. I don't know if you're familiar. I mean, you guys all know about them because you're seeing them for rheumatoid arthritis, but there's very interesting data that the JAK pathway appears to be relevant. And when given systemically, they've warped. But the problem's then when they tried to convert those topically. There's two companies, they're working in this area in relatively large and early work in Phase 2A's, studies the drug has actually not worked as well as people would've liked. Part of that has to do with where the hair follicle is. It's a deep structure. It lives down below the dermis in the subcu, or deep in the dermis. And getting a drug to penetrate that far deep down into skin is really difficult.

DER_02: So I never used it because when I was taking care of these patients with alopecia areata, I found topical steroids or intralesional steroids to be more effective. I actually didn't have a lot of those patients and I just did not think that there was sufficient data to warrant sensitizing somebody to this drug or this particular chemical, even though it's not a chemical you're likely you're going to run into in the general world. I just didn't find there was enough evidence to support its use. But if you want, to people who are predominantly just taking care of a lot of these patients with hair loss who are pretty desperate, there may be some people who are more comfortable with it and would probably want to try it. But that's just because if you look up the treatment for alopecia areata, you see 100 things on the list. That's because we don't have anything that works very well and people get desperate.

Interviewer 1.: Okay. So with alopecia areata, is it a treatable condition or is it mostly just like you manage it until the hair loss happens again? Or ...

DER_02: Right. So different people have different manifestations of the disease. Some people will have a fairly benign course where they have patchy alopecia that will respond to treatment and will go away. Others will progress and when you get loss of hair in the occipital area, which is a condition called ophiasis where you get progression to involve the total scalp, the eyebrows, the eyelashes. Those people tend to not do well. The longer they've had the disease, the harder it is to treat. And there are ... There's a very, very, very active and wonderful patient advocacy group that actually does a lot of work to help support patients and their families who have this disorder and try to help. [inaudible 00:11:01] that some of these are kids, and they can be ... Kids can be cruel.

Interviewer 1.: Yeah. So you had mentioned that you haven't used this in your practice. Do you know anybody that has used it or has been intrigued, I guess, by the potential for use?

DER_02: Because I spent a large part of my life in academic medicine and I'm still on the boards for a couple of our professional organizations that have a pretty strong network, I do know, I refer to them essentially as the hair mafia. [redacted]. There are people who take care of a lot of hair loss patients because for many of us, they're hard patients to take care of because we don't have good treatment options. If it's a component of what you

guys would like to do is have me ask some of these other people what their thoughts are on how much they're using or what they're currently doing for alopecia areata patients, I certainly can get in touch with them and they'd be happy to provide some additional information.

Interviewer 1.: Yeah. That could be great. Yeah. Because I think what we're trying to figure out is, is there a clinical need for this particular substance? And that's a pretty broad category of what do you consider a need. So we're looking to see maybe it's ... Some of the substances, maybe it's a first-line. We reviewed one substance previously that's used in ophthalmology and it's actually one of the safer substances compared to some of the other dyes that they use for this particular procedure.

Interviewer 1.: And like you had said, with these types of patients, maybe we don't have a lot of good things to work. So is it one of those I've tried everything else, let me just try this and see what happens kind of a thing? To where we want to capture that to make sure that we can put together this comprehensive picture of maybe it's not necessarily a first-line, but it's one of these that if you were to get rid of it or you were going to exclude people from being able to use it, would it affect a pretty good amount of people that are already dealing with probably pretty stigmatizing disease because they've lost all of their hair? So we want to make sure that we're capturing as much information as we can.

DER_02: Yeah. And my bet would be, particularly with what's recently been happening in this field, I will tell you in my 30-odd years in dermatology, nobody has been as ginned up and as excited as what is happening right now with the JAK inhibitors. They are really rocking the alopecia areata world. And it's a really interesting story because it actually mechanistically makes a lot of sense from what we know about the pathway. So that, and then they are already being approved for other indications. So they're coming to the market. Every pharmaceutical company and their brother has got one of these drugs. And you guys can look them up. I'm sure you're well aware there's about six or more of these in development for varying indications. So there's some already out there, plus more coming. But the [inaudible 00:14:22] oral data was pretty compelling when it first came out, and it really did garner a lot of enthusiasm. I think that the story is still to be writ. I want to just back up a bit, Ashlee, because I understood also is that this is really about bulk substance, right?

Interviewer 1.: Yes. Yes.

DER_02: Okay. So even if from a bulk substance perspective we say this is not a drug for which there's a huge market or a huge need, and if it was to disappear in the bulk substance world, a physician could still potentially write for it and have it be compounded. Correct?

Interviewer 1.: So there is a separate list for 503A facilities, which is your typical compounding pharmacy. And so there is going to essentially be the same sort of list comprised of what you can use from a bulk standpoint. We're only looking at the outsourcing facilities component, but there is a separate regulation regarding the 503A's. However, there is a little bit different. So with the outsourcing facilities, it's either on this list as a bulk or it's not used at all. If there's a USP monograph, a 503A compounding pharmacy can still use it. So there's a little bit less restrictions or a little bit more options that a 503A could potentially do. And so there is the potential, but if there is a USP monograph, then it

would still be allowed even if it doesn't end up on this list. So there still could be the potential that they would be able to get it, yes.

DER_02: Right. And I think ... So from a historical perspective, back in 1980's is when we heard about this and said, "Oh this would be, gee willikers, a great way to treat alopecia areata or patients with widespread warts or widespread [inaudible 00:16:32]. The same premise that you're going to be tickling the immune system in a way that you're stimulating the normal immune response to kick in in a way that the pathway's been altered. But in the more recent post-2000 era, I think the use of this particular product has been somewhat marginalized.

Interviewer 1.: Okay.

DER_02: That would be my ... That's my take. Just by perspective of the history of when did I hear about it and what did we know about it.

Interviewer 1.: Yeah. So you had mentioned previously that to get into where the hair follicle is, it's kind of complicated from a topical application. So what we had found mostly was that this was used as a solution that's been dissolved in acetone. So I guess in terms of actually penetrating down to the hair follicle, is that something that this substance would need to do, or is it just serving as an irritant almost?

DER_02: No, it's actually serving as a sensitizer. So you're putting it on to induce an immune response. In skin ... Oh, all this is like how I spent the first half of my life. Skin actually has resident T cells and antigen-presenting cells in it. So when you put a hapten like this compound on the surface of the skin, it actually will bond to protein cells on the surface of the skin and get presented and turn on an immune response. A classic example is poison ivy, okay? It's a hapten you get on your skin. The first time you see it, nothing happens. The second time, you come back and now you're going to generate an immune response that's directed against that hapten.

DER_02: The goal here is not for the drug to penetrate down into the hair follicle. The goal here is that you're going to stimulate an immune response and you're going to bring in these T cells that are now directed against the DCP and get directed against that, and maybe the cells that were targeting the hair follicle are going to be distracted from the hair follicle attack and are going to instead be responding to the topical DCP. So in this particular instance, the drug doesn't have to get down into the hair follicle. It's actually happening at the surface of the skin within the epidermis and the dermis.

DER_02: With other drugs where we're trying to actually direct therapy to try to target and shut off an immune response or get rid of that activation or that immunologic process, there's where we're trying to drive drugs to get deeper in the skin. The general rule for drug development in dermatologics is things that are over 500 Daltons will tend to penetrate through the epidermis and things that are bigger than that don't get through very much. But I can point to a heck of a lot of drugs that are up to 1,000 Daltons that are still having an activity that is clearly below the epidermis, way in the dermis.

Interviewer 1.: Okay. So I guess in terms of ... I guess for all the other indications that it lists, is it kind of the same sort of a process of creating that immune reaction?

DER_02: Right. Right. Warts and molluscum are both viral infections. So is verruca plana. Verruca plana are flat warts. They're small, minimally elevated warts that are widespread across

the face and they're difficult to treat because they're small, very [inaudible 00:20:19], not well circumscribed, and people will be loaded with them. So somebody's who's got flat warts can have 50 or 100. And the current therapy for generally most of the viral infections are destructive therapies, so liquid nitrogen or cryotherapy or curettage and desiccation. And if you've got a kid who's got flat warts, you don't want to have to curette off or try to freeze all those warts. Same thing with molluscum. So the idea here would've been oh, well let's try to do this. But I don't think it makes any sense.

DER_02: The problem with warts is they are localized only within the epithelium. They're at the farthest reaches of the immune response. Your body doesn't see that as something foreign. It doesn't respond to it, particularly in immunocompromised patients. So patients who've got cancer, patients who are HIV-positive, there's a lot more viral infections. AIDS patients also get herpes, and any patient on a chemotherapeutic regimen, there's a high risk for both HSV as well as warts. But I never used it because I never thought it, again, that it made a lot of sense from an immunology perspective. I'm going to give somebody a contact dermatitis, essentially, but that doesn't mean that their wart's going to get worse. If anything, I'm worried they're going to start scratching and they're going to distribute these and auto-inocculate. So I didn't think this was a good idea.

Interviewer 1.: Okay. That's very interesting. So I guess in terms of ... You had kind of mentioned the writing the prescription. Is there any reason that you would see this particular substance as something that, as a dermatologist, you would want to stock in your office, or would it be something that you would write and you would have the patient administer it at home?

DER_02: Good question. As I understood it ... There's two phases to this. There's the induction phase and then the [inaudible 00:22:34], which is when you're going to be generating an immune response, and then there's the part where people are treating. And I don't remember the ... I think that the doses that were used were slightly different, and it could have been that people ... In the old, old days, I trained with a guy [redacted]. And I think he may have had this around where he was applying it to sensitize people in the office, but then writing a prescription with a lower strength. But again, I'd have to go back and look at it. It's been a while. I'm talking like 1982, right?

Interviewer 1.: Yeah. Because I think from what we had gathered from our literature search was there was a 2% solution that would be applied as a sensitizer, and then the patient would return either one or two weeks later and then it would be evaluated on whether or not a mild dermatitis had been elicited. If it had been, then they would write concentrations, I think we saw concentrations for anywhere like .0001% all the way up through 5%. And they would have these various concentrations depending on the type of reaction that the patient had. So if it wasn't a very severe reaction, they'd increase the strength. If it was a severe reaction, they'd decrease it. So it seemed like it was a little bit all over the place in terms of normal dosing and things like that to where I didn't know if it would make more sense for it to be administered in the office. Because that way, as a prescriber, you can have all these various concentrations, you apply it, and then the patient comes back versus having to write seven different prescriptions for a patient to go pick up this compounded product.

DER_02: No. So this is where the art comes in. And I'm looking at something online, so I've actually ... Some of my good friends in New Zealand who have a wonderful website, so I'm remembering correctly. So there would be a dose concentration that would be used in

the office. But again, it's like that first exposure to poison ivy. That's the highest concentration. They would put it on and then they would write for the lower. I think this is where the art of everybody would pick what they thought they needed to use. And it's not an irritant dermatitis, it's actually allergic contact dermatitis that you're trying to induce. They give it deliberately sensitizing somebody to the chemical.

DER_02: And this is part of the difference between this kind of work and what the kind of work that I like to do. We can say that there's an infinite number of doses and what you have to do is pick the dose that's safe and effective. I don't think there's been great data that supports the efficacy that sort of makes me think do we need to keep this around and what is it that we're ... In some ways, having this available keeps people from reaching for something that may actually work.

Interviewer 1.: Yeah. Okay. That's interesting. So I guess in terms of ... And I think maybe this doesn't have any sort of impact. I think we had found a couple of them would use it in terms of a topical solution and then others would use it in an acquiesce cream sort of a base. From your standpoint, would that make any difference in terms of eliciting the reaction?

DER_02: No. Once you have put the first on and you've gotten the patient sensitized, whether you use a solution or the cream should not really matter. The real issue would be how long is the product stable for? So I don't know enough about this particular compound. I haven't seen its structure. But going back to our old pharmacy days of is it stable in water, or is it stable in an ointment, or is somebody putting it up in Aquaphor, or what the heck happened to it, and how well can you maintain the stability of the product, what's the shelf life, what are the breakdown products, et cetera.

Interviewer 1.: Okay. So-

DER_02: It must not be particularly soluble if you're putting it in acetone.

Interviewer 1.: Yeah. I think from what we had gathered, and I haven't looked at the chemical structure, either. But from what we have gathered, it is more soluble in acetone as compared to ... There's another one that they had studied. I'm trying to think. There was three of the contact sensitizers, there was an SADBE, there was this diphenylcyclopropenone, and then there was a third one. And I think this one was more soluble than one of the other ones and then it's cheaper than the SADBE one, which is why this one seemed to have had become the favorite, I guess, amongst the articles that we had been reading.

Interviewer 1.: But no, my assumption ... I don't know if the acetone would play any role in enhancing the effect of the sensitizer or if it was just because that's the only thing it was soluble in. That part of it I'm not entirely sure. It seemed like there was a couple articles that, I think they were all maybe from the same author, where they actually put it in an acquiesce cream base. And I don't know if maybe because it's more acceptable for a patient or I don't know what the reasoning behind all of that was. We're still trying to decipher all of these intricacies out as we move along.

DER_02: The one thing about acetone is it would volatilize really quickly. So if you put it on in acetone, it's going to slash off pretty fast and you'd be left with the drug itself left on the surface of the skin, whereas if you put it into something like Aquaphor or an acquiesce cream Eucerin, you're potentially going to have a little bit more of the drug potentially residual on the surface. Maybe.

Interviewer 1.: Okay. So I guess in terms of the office use versus the application at home, would you have any concerns about a patient applying it at home to sensitizing other people around them?

DER_02: No, because what they were doing was using the highest concentration at the office to do the sensitization. Now you could potentially inadvertently sensitize somebody, but it's not a compound that's around in the environment that is going to cause major, significant problem. People are more likely to be sensitized to nickel and chromates and all kinds of other chemicals that we're in daily contact with. Or we get irritant contact dermatitis. People who have soap residue under their wedding ring and every time they're washing their hands a lot, they get a rash under their ring. But that's an irritant, that's not an allergic contact dermatitis. I'm not worried about that. I am somewhat more worried about the safe use in the context of where the heck did they put it. Could you get it all over you in a way that leads to a reaction that's not going to be great? It's a classic type for delayed hypersensitivity reaction. It's not an anaphylactic reaction, it's not an IgE mediated thing, but it's still generally not a good idea. People with widespread contact dermatitis can be pretty uncomfortable.

Interviewer 1.: Yeah. So out of all of the different indications, is your medical expert opinion that there really isn't strong evidence for use in any of the indications?

DER_02: Correct. I think the only other ... You know what, I knew about this particularly for alopecia areata, rumors about its use in warts or viral infections, including verruca plana, but I don't think it's great. Sorry. I've been traveling and I came down with something [inaudible 00:30:51].

Interviewer 1.: Yeah. It's about that time of the season, too.

DER_02: But the other indications are really, I think, not good. And they may have been ... My guess is these are reports that probably go back to ancient history, right? Like 10 or 20 years ago?

Interviewer 1.: They-

DER_02: Melanoma. We didn't have any great drugs for melanoma until about 10, 15 years ago. Now we've got bucket loads.

Interviewer 1.: Yeah. I don't remember how old those articles were, but they were mostly case reports of a patient who maybe failed multiple different treatment options and then they tried this, and they had beneficial results. But it's nothing overwhelmingly compelling that randomized controlled trials show that it was effective.

DER_02: Right. And then when 20 other people reported repeated that and didn't get a response, those don't get published.

Interviewer 1.: Yeah. Exactly. So let me double check my questions that I have for you. So I guess we had done a little bit of our literature had shown this discussion between whether or not it should be used in children versus adults. Is there any reason that you could think why a particular patient population ... Would you want to avoid it in kids because of the side effects, or would it be okay in a child, or is there any sort of patient population that you would be extremely concerned about, aside from all the it may not even be that effective at all?

DER_02: That's a really good question. I think particularly lots of my work has been about kids and safety. Is there any additional worth to kids? I don't know. I think it's an ethical issue in the context of offering a patient and a family member treatment for which there's not data to support it's likely to be effective. And if you offer a treatment that's not effective, are you keeping somebody from potentially getting to something that is effective? How do you do informed consent? My friend the oncologist always says it's an oxymoron when it comes to cancer. If you have a kid with hair loss and the doctor says, "We might try this. It might work," how are you going to know? Somebody is offering that to you, maybe you think that they must know something and it will work, even though there's not good data to say that it will.

Interviewer 1.: Yeah. Okay.

DER_02: I am always more concerned about kids. There's a higher standard that goes into clinical trial development. You have to have data to say that something has a benefit before you're allowed to proceed into dosing children.

Interviewer 1.: Yeah.

DER_02: That being said, the counterargument would be well, you know that (Topricin?) and those other drugs are not working very well topically, so if I use this topically and I avoid systemic administration of the drug, there may be some concerns. The JAK's and the STAT's, they had some unpleasant side effects that have to be monitored. We don't know a lot about them yet.

Interviewer 1.: Yeah. So you had mentioned ... So a lot of the stuff that you had mentioned was back several years ago where this was around when you were training at that one site that you trained at. So would you say that, from your perception, it's almost fallen out of favor because we have more effective or just more several different options for treatment?

DER_02: Yeah. I think in the context of alopecia areata that is likely to be true. Nothing that has actually been approved ... Dermatology is an interesting field. We have 2,000-plus diseases and only about 10 diagnoses that have a large enough market size that things are actually get through the approval process. So alopecia areata has, up until relatively recently, not been a disease for which there's been a lot of drug development activity ongoing, or even clinical trials. So we've had topical steroids, we've got topical steroids in every flavor, in [inaudible 00:35:33], in creams, in ointments. They're not approved, per se, for alopecia areata. They're approved for inflammatory skin diseases, and that's usually what their label says. But alopecia areata fits in that category, and that's how they get used.

Interviewer 1.: Okay. So one of my questions was why would you use this substance over an FDA-approved product, but it sounds like there really aren't that many FDA-approved products, and it sounds like you wouldn't use this over any of those other options, so.

DER_02: And that's the one, it came to me. The other one that used to be used was DNCB, dinitrochlorobenzene.

Interviewer 1.: Yep. That was it. Yep.

DER_02: Oh, look at that. I remembered.

Interviewer 1.: So I guess in terms of side effects. So the biggest ... So we're trying to be careful with, as we're collecting our information, we're not trying to determine whether or not it's a safe and effective product, because then that kind of implies that it should go through the FDA approval process and all of that. So I guess if somebody were to use this product, what would be the biggest side effect or adverse effect that you could anticipate from this?

DER_02: Well the treatment effect is what you are doing in inducing contact dermatitis. So you are going to get an allergic contact dermatitis. That's the goal. The goal is to induce that AECB, allergic eczematous contact dermatitis, in order to potentially stimulate the hair to regrow. So that will be ... You get the redness, the itching, oozing. They may get secondarily infected. But you're developing something that essentially looks like poison ivy, potentially in a mild form. But that's the art of picking the right concentration. By the way, it's not that the concentration is so critical, it's really about the individual patient. My guess, if I came in with poison ivy to that room where the four of you are sitting and put each one of you, you're all going to have a slightly different response. Not necessarily because I've got the dose different, but because your immune response is going to be different depending on how much exposure you previously had and just how twitchy you are, from an immunologic perspective.

Interviewer 1.: Yeah. Okay. I think those were pretty much all of the questions that we had for you. Is there anything else that you think we need to explore, or any different resources that you think we need to look into in regard to this particular substance?

DER_02: No. [redacted]. Is DNCP on your list? Because if you're doing DPCP, I imagine DNCP might be the other one.

Interviewer 1.: So right now we only have 10 substances that we're reviewing. So we have our full proposal that's been approved and we've received funding for it, we're just waiting for the FDA to give us the list of substances that we're going to review next. Because we're essentially going to be doing 75 a year for the next three years, so it's possible that one will be on our list but as of right now, it's just this diphenylcyclopropenone one that we have.

DER_02: Okay. I will ask. The derm community, some of them may be more familiar with DNCP, which is the one that I remembered. But let's just ask.

Interviewer 1.: Okay. Yeah. That would be great. Yeah. I think our biggest concern is that we're going to miss something, so we definitely want to make sure that we're not missing anything in terms of its use. And it's interesting because most of the studies that we've been reading in our literature review were not done in the United States. I think only a handful of them are from the United States. And so I'd be curious just to see from kind of like an international perspective if this is one of those things that has fallen out of favor in the United States, or other countries use it because maybe they don't have as many options as we do. I don't really know.

DER_02: I don't think so. [redacted]. I think these other indications, vitiligo, pre-transplant sensitization, et cetera, just seemed really one-off and not high of use. Vitiligo's the other one that's very closely related to alopecia from a mechanistic standpoint where you're targeting immune cell to target melanocytes and people end up with patches of white on their skin, which ... There are a lot of things that are being used to try to address that, also. Back to that same issue with the JAK's [inaudible 00:40:54] inhibitors.

Interviewer 1.: Yeah. Okay. I think those were all the questions. Did you all have any other questions? Did I miss anything from your... So I guess in terms of some next steps. So we're going to be continuing to reach out to other dermatologists and if you have any that you could recommend that maybe we could talk to about this substance as well. We're limited right now to where we can only consult with nine people until we get our waiver from the FDA to reach out to more people. But our final goal is initially to send out a comprehensive survey to different dermatologists across the country just to get more of an idea of how it's used on this broader scale. And so we would hope that you would be able to help us out as we go through this process. [redacted] But working with them to make sure that we're not missing any indication, this is what we've found so far. The answers that you've given us are extremely helpful as we're not dermatologists. We're trying to decipher a lot of the things that we have, so we appreciate your help and hope that you'll help us as we continue through this process to identify people that we might be of interest for us to talk to throughout this whole project.

DER_02: Right. And I think the key is ... Look, there are 12,000 dermatologists in the U.S. I'm sure I could find somebody thinks this is good. That doesn't only mean there's data that supports safety and efficacy.

Interviewer 1.: Yeah. And I think that part of it is also not just the ... If somebody wants to write a prescription for it, that's completely fine. That's not within the scope of what we're doing. We're looking at the bigger picture of why does this need to be done by an outsourcing facility, why does it need to be compounded in bulk, why do we need to start from the bulk substance, what's that reasoning to why ... If a patient comes in, is it an emergency where you need to apply this, or is it something that-

DER_02: No. No.

Interviewer 1.: ... a prescript-

DER_02: N-O. It is not an emergency ever.

Interviewer 1.: Okay. So this theoretically could be something that, even for the sensitization, you could write a prescription for. The patient picks it up, bring it to you in the office and you apply it, and then they come back?

DER_02: Correct.

Interviewer 1.: Okay. Okay. That's it.

DER_02: Or you write the prescription and you get it sent to your office.

Interviewer 1.: Okay. And then you just have it for that particular patient?

DER_02: For that one patient, right. Unless there's somebody out there who is running a mill, we won't even go there. But look, there are unethical people who think they can make money, and I'm not interested in supporting that kind of activity. Again, in the absence of good data to support its use, they want to potentially put patients at risk.

Interviewer 1.: Yeah. Okay. Well I think that was everything that we had for you, and I'm sure we will be in touch as we work through all of this and try to decipher all the information that we have. I really appreciate you taking the time this afternoon to talk with us.

DER_02: Happy to do it. I love the intersection of new compounds and compounding in pharmacy, in dermatology, and drug development. They've all been my favorite topic.

Interviewer 1.: Oh, good. Because I'm sure we will have all sorts of dermatology products as we move through this because it's a huge area. So thank you so much and enjoy the rest of your afternoon.

DER_02: Thank you. Bye bye.

Interviewer 1.: Alright. Bye.

INTERVIEW_NAT_01B

Interviewer 1: Okay. So, I guess since you use those, the other two were Brilliant blue and diphenylcyclopropenone (DPCP). Just to cover all the bases, do you use those two at all?

NAT_01B: Not on purpose.

Appendix 3. Survey instrument

Start of Block: Welcome Page

The University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI), in collaboration with the Food and Drug Administration (FDA), is conducting research regarding the use of certain bulk drug substances nominated for use in compounding by outsourcing facilities under section 503B of the Federal Food, Drug, and Cosmetic Act. In particular, we are interested in the current and historic use of these substances in clinical practice. This survey is for **diphenylcyclopropenone (DPCP)**. As a medical expert, we appreciate your input regarding the use of this substance in your clinical practice. This information will assist FDA in its development of a list of bulk drug substances that outsourcing facilities can use in compounding under section 503B of the Act. All responses are anonymous.

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

The time required to complete this information collection is estimated to average 30 minutes, including the time to review instructions, search existing data sources, gather the data needed, and complete and review the information collection. 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. If you have additional questions or concerns about this research 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.

End of Block: Welcome Page

Start of Block: Diphenylcyclopropenone (DPCP)

Q1. What type(s) of product(s) do you use, prescribe, or recommend for **diphenylcyclopropenone (DPCP)**? Please check all that apply.

- ☐ Compounded drug product
- ☐ FDA-approved drug product
- ☐ Over the counter drug product
- ☐ Dietary supplement (e.g. vitamin or herbal supplement products sold in retail setting)
- ☐ Unsure

Skip To: Q13. If What type(s) of product(s) do you use, prescribe, or recommend for substance? Please check all th... != Compounded drug product Is Not Selected

Skip To: Q2. If What type(s) of product(s) do you use, prescribe, or recommend for substance? Please check all th... = Compounded drug product Is Selected

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Display This Question:

If What type(s) of product(s) do you use, prescribe, or recommend for substance? Please check all th... = Compounded drug product

Q2. Please list any conditions or diseases for which you use compounded **diphenylcyclopropenone (DPCP)** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

	Strength(s) (please include units)	Dosing frequency(ies)	Dosage form(s)	Route(s) of administration	Duration of therapy	Patient population
Condition 1 (please describe)						
Condition 2 (please describe)						
Condition 3 (please describe)						
Condition 4 (please describe)						
Condition 5 (please describe)						

Q3. Do you use compounded **diphenylcyclopropenone (DPCP)** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

- ☐ Single
- ☐ Combination

Skip To: Q5. If Do you use compounded substance as a single agent active ingredient, or as one active ingredient... != Combination Is Not Selected

Display This Question:

If Loop current: Do you use compounded substance as a single agent active ingredient, or as one active ingredient... = Combination Is Selected

Q4. Please list all combination products in which you use compounded **diphenylcyclopropenone (DPCP).**_____

Q5. For which, if any, diseases or conditions do you consider compounded **diphenylcyclopropenone (DPCP)** standard therapy?_____

Q6. Does your specialty describe the use of compounded **diphenylcyclopropenone (DPCP)** in medical practice guidelines or other resources?_____

Q7. Over the past 5 years, has the frequency in which you have used compounded diphenylcyclopropenone (DPCP) changed?

- o Yes - I use it **MORE** often now (briefly describe why) _____
- o Yes - I use it **LESS** often now (briefly describe why) _____
- o No - use has remained consistent

Q8. Why do you use compounded **diphenylcyclopropenone (DPCP)** instead of any FDA-approved drug product? _____

Q9. Do you stock non-patient-specific compounded **diphenylcyclopropenone (DPCP)** in your practice location?

- Yes
- No

Skip To: End of Block If Do you stock non-patient-specific compounded substance in your practice location? = No

Display This Question:

If Do you stock non-patient-specific compounded substance in your practice location? = Yes

Q11. In what practice location(s) do you stock non-patient-specific compounded **diphenylcyclopropenone (DPCP)** ? Please check all that apply.

- ☐ Physician office
- ☐ Outpatient clinic
- ☐ Emergency room
- ☐ Operating room
- ☐ Inpatient ward
- ☐ Other (please describe) _____

Q12. How do you obtain your stock of non-patient-specific compounded **diphenylcyclopropenone (DPCP)** ? Please check all that apply.

- ☐ Purchase from a compounding pharmacy
- ☐ Purchase from an outsourcing facility
- ☐ Compound the product yourself
- ☐ Other (please describe) _____

Q13. Why do you keep a stock of non-patient-specific compounded **diphenylcyclopropenone (DPCP)** ? Please check all that apply.

- ☐ Convenience
- ☐ Emergencies
- ☐ Other (please describe) _____

Skip To: End of Block If Why do you keep a stock of non-patient-specific compounded substance? Please check all that apply. = Convenience

Skip To: End of Block If Why do you keep a stock of non-patient-specific compounded substance? Please check all that apply. = Emergencies

Skip To: End of Block If Why do you keep a stock of non-patient-specific compounded substance? Please check all that apply. = Other (please describe)

Q14. For which, if any, diseases or conditions do you consider **diphenylcyclopropenone (DPCP)** standard therapy?

_____

Q15. Does your specialty describe the use of **diphenylcyclopropenone (DPCP)** in medical practice guidelines or other resources?

_____

End of Block: Diphenylcyclopropenone (DPCP)

Start of Block: Background Information

Q16. What is your terminal clinical degree? Please check all that apply.

- ☐ Doctor of Medicine (MD)
- ☐ Doctor of Osteopathic Medicine (DO)
- ☐ Doctor of Medicine in Dentistry (DMD/DDS)
- ☐ Naturopathic Doctor (ND)
- ☐ Nurse Practitioner (NP)
- ☐ Physician Assistant (PA)
- ☐ Other (please describe) _____

Q17. Which of the following Board certification(s) do you hold? Please check all that apply.

- ☐ No Board certification
- ☐ Allergy and Immunology
- ☐ Anesthesiology
- ☐ Cardiovascular Disease
- ☐ Critical Care Medicine
- ☐ Dermatology
- ☐ Emergency Medicine
- ☐ Endocrinology, Diabetes and Metabolism
- ☐ Family Medicine
- ☐ Gastroenterology
- ☐ Hematology
- ☐ Infectious Disease
- ☐ Internal Medicine
- ☐ Medical Toxicology
- ☐ Naturopathic Doctor
- ☐ Naturopathic Physician
- ☐ Nephrology
- ☐ Neurology
- ☐ Obstetrics and Gynecology
- ☐ Oncology
- ☐ Ophthalmology
- ☐ Otolaryngology
- ☐ Pain Medicine
- ☐ Pediatrics
- ☐ Psychiatry
- ☐ Rheumatology
- ☐ Sleep Medicine
- ☐ Surgery (please describe) _____
- ☐ Urology
- ☐ Other (please describe) _____

End of Block: Background Information

Appendix 4. Raw survey data

See attached PDF for raw survey data.

Q144.
The University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI), in collaboration with the Food and Drug Administration (FDA), is conducting research regarding the use of certain bulk drug substances nominated for use in compounding by outsourcing facilities under section 503B of the Federal Food, Drug, and Cosmetic Act. In particular, we are interested in the current and historic use of these substances in clinical practice.

There are **twelve (12)** substances contained in this survey. As a medical expert, we appreciate your input regarding the use of these substances in your clinical practice. This information will assist FDA in its development of a list of bulk drug substances that outsourcing facilities can use in compounding under section 503B of the Act. All responses are anonymous.

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

The time required to complete this information collection is estimated to average 30 minutes, including the time to review instructions, search existing data sources, gather the data needed, and complete and review the information collection. 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.

If you have additional questions or concerns about this research 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.

Q1. Which of the following substances do you use in your practice? Please check all that apply.

- [ ] Amphotericin B
- [ ] Boric acid
- [x] Cantharidin
- [x] Ciclopirox olamine
- [ ] Clioquinol
- [ ] Deoxy-d-glucose
- [ ] Diiodohydroxyquinoline
- [ ] Diphenylcyclopropenone (DPCP)
- [ ] Podophyllum
- [x] Podophyllum resin
- [x] Quinacrine
- [x] Squaric acid dibutyl ester (SADBE)
- [ ] None of the above

Q2. What type(s) of product(s) do you use, prescribe, or recommend for **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q3. Please list any conditions or diseases for which you use compounded **amphotericin B** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q4.

Do you use compounded **amphotericin B** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q5. Please list all combination products in which you use compounded **amphotericin B**.

This question was not displayed to the respondent.

Q6. For which, if any, diseases or conditions do you consider compounded **amphotericin B** standard therapy?

This question was not displayed to the respondent.

Q7. Does your specialty describe the use of compounded **amphotericin B** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q8. Over the past 5 years, has the frequency in which you have used compounded **amphotericin B** changed?

This question was not displayed to the respondent.

Q9. Why do you use compounded **amphotericin B** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q10. Do you stock non-patient-specific compounded **amphotericin B** in your practice location?

This question was not displayed to the respondent.

Q11. In what practice location(s) do you stock non-patient-specific compounded **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q12. How do you obtain your stock of non-patient-specific compounded **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q13. Why do you keep a stock of non-patient-specific compounded **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q14. For which, if any, diseases or conditions do you consider **amphotericin B** standard therapy?

This question was not displayed to the respondent.

Q15. Does your specialty describe the use of **amphotericin B** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q388. What type(s) of product(s) do you use, prescribe, or recommend for **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q389. Please list any conditions or diseases for which you use compounded **boric acid** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q390.
Do you use compounded **boric acid** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q391. Please list all combination products in which you use compounded **boric acid**.

This question was not displayed to the respondent.

Q392. For which, if any, diseases or conditions do you consider compounded **boric acid** standard therapy?

This question was not displayed to the respondent.

Q393. Does your specialty describe the use of compounded **boric acid** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q394. Over the past 5 years, has the frequency in which you have used compounded **boric acid** changed?

This question was not displayed to the respondent.

Q395. Why do you use compounded **boric acid** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q396. Do you stock non-patient-specific compounded **boric acid** in your practice location?

This question was not displayed to the respondent.

Q397. In what practice location(s) do you stock non-patient-specific compounded **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q398. How do you obtain your stock of non-patient-specific compounded **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q399. Why do you keep a stock of non-patient-specific compounded **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q400. For which, if any, diseases or conditions do you consider **boric acid** standard therapy?

This question was not displayed to the respondent.

Q401. Does your specialty describe the use of **boric acid** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q402. What type(s) of product(s) do you use, prescribe, or recommend for **cantharidin**? Please check all that apply.

- [x] Compounded drug product
- [ ] FDA-approved drug product
- [ ] Over the counter drug product
- [ ] Dietary supplement (e.g. vitamin or herbal supplement products sold in retail setting)
- [ ] Unsure

Q403. Please list any conditions or diseases for which you use compounded **cantharidin** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

	Strength(s) (please include units)	Dosing frequency(ies)	Dosage form(s)	Route(s) of administration	Duration of therapy	Patient population
Condition 1 (please describe): Molluscum contagiosum	0.7%	q2wks	liquid	topical	Until resolved	Pediatric
Condition 2 (please describe): Verruca plana	0.7%	q2wks	liquid	topical	Until resolved	Pediatric / Adult
Condition 3 (please describe)						
Condition 4 (please describe)						

Condition 5 (please describe)

Condition 6 (please describe)

Condition 7 (please describe)

Condition 8 (please describe)

Q404.
Do you use compounded **cantharidin** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

- [x] Single
- [ ] Combination

Q405. In which combination(s) do you use compounded **cantharidin**? Please check all that apply.

This question was not displayed to the respondent.

Q406. For which, if any, diseases or conditions do you consider compounded **cantharidin** standard therapy?

Molluscum contagiosum

Q407. Does your specialty describe the use of compounded **cantharidin** in medical practice guidelines or other resources?

Yes

Q408. Over the past 5 years, has the frequency in which you have used compounded **cantharidin** changed?

- (•) Yes - I use it **MORE** often now (briefly describe why) More pediatric patients
- ( ) Yes - I use it **LESS** often now (briefly describe why)
- ( )

No - use has remained consistent

Q409. Why do you use compounded **cantharidin** instead of any FDA-approved drug product?

Painless. High degree of efficacy. Reduced risk of scarring. Applied in office / controlled setting.

Q410. Do you stock non-patient-specific compounded **cantharidin** in your practice location?

- (•) Yes
- ( ) No

Q411. In what practice location(s) do you stock non-patient-specific compounded **cantharidin**? Please check all that apply.

- [x] Physician office
- [x] Outpatient clinic
- [ ] Emergency room
- [ ] Operating room
- [ ] Inpatient ward
- [ ] Other (please describe)

Q412. How do you obtain your stock of non-patient-specific compounded **cantharidin**? Please check all that apply.

- [x] Purchase from a compounding pharmacy
- [ ] Purchase from an outsourcing facility
- [ ] Compound the product yourself
- [ ] Other (please describe)

Q413. Why do you keep a stock of non-patient-specific compounded **cantharidin**? Please check all that apply.

- [x] Convenience
- [ ] Emergencies
- [ ] Other (please describe)

Q414. For which, if any, diseases or conditions do you consider **cantharidin** standard therapy?

This question was not displayed to the respondent.

Q415. Does your specialty describe the use of **cantharidin** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q416. What type(s) of product(s) do you use, prescribe, or recommend for **ciclopirox olamine**? Please check all that apply.

- [ ] Compounded drug product
- [x] FDA-approved drug product
- [ ] Over the counter drug product
- [ ] Dietary supplement (e.g. vitamin or herbal supplement products sold in retail setting)
- [ ] Unsure

Q417. Please list any conditions or diseases for which you use compounded **ciclopirox olamine** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q418.
Do you use compounded **ciclopirox olamine** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q419. In which combination(s) do you use compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q420. For which, if any, diseases or conditions do you consider compounded **ciclopirox olamine** standard therapy?

This question was not displayed to the respondent.

Q421. Does your specialty describe the use of compounded **ciclopirox olamine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q422. Over the past 5 years, has the frequency in which you have used compounded **ciclopirox olamine** changed?

This question was not displayed to the respondent.

Q423. Why do you use compounded **ciclopirox olamine** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q424. Do you stock non-patient-specific compounded **ciclopirox olamine** in your practice location?

This question was not displayed to the respondent.

Q425. In what practice location(s) do you stock non-patient-specific compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q426. How do you obtain your stock of non-patient-specific compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q427. Why do you keep a stock of non-patient-specific compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q428. For which, if any, diseases or conditions do you consider **ciclopirox olamine** standard therapy?

Onychomycosis, tinea pedis

Q429. Does your specialty describe the use of **ciclopirox olamine** in medical practice guidelines or other resources?

Yes

Q430. What type(s) of product(s) do you use, prescribe, or recommend for **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q431. Please list any conditions or diseases for which you use compounded **clioquinol** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q432.
Do you use compounded **clioquinol** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q433. In which combination(s) do you use compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q434. For which, if any, diseases or conditions do you consider compounded **clioquinol** standard therapy?

This question was not displayed to the respondent.

Q435. Does your specialty describe the use of compounded **clioquinol** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q436. Over the past 5 years, has the frequency in which you have used compounded **clioquinol** changed?

This question was not displayed to the respondent.

Q437. Why do you use compounded **clioquinol** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q438. Do you stock non-patient-specific compounded **clioquinol** in your practice location?

This question was not displayed to the respondent.

Q439. In what practice location(s) do you stock non-patient-specific compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q440. How do you obtain your stock of non-patient-specific compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q441. Why do you keep a stock of non-patient-specific compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q442. For which, if any, diseases or conditions do you consider **clioquinol** standard therapy?

This question was not displayed to the respondent.

Q443. Does your specialty describe the use of **clioquinol** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q444. What type(s) of product(s) do you use, prescribe, or recommend for **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q445. Please list any conditions or diseases for which you use compounded **deoxy-d-glucose** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q446.
Do you use compounded **deoxy-d-glucose** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q447. In which combination(s) do you use compounded **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q448. For which, if any, diseases or conditions do you consider compounded **deoxy-d-glucose** standard therapy?

This question was not displayed to the respondent.

Q449. Does your specialty describe the use of compounded **deoxy-d-glucose** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q450. Over the past 5 years, has the frequency in which you have used compounded **deoxy-d-glucose** changed?

This question was not displayed to the respondent.

Q451. Why do you use compounded **deoxy-d-glucose** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q452. Do you stock non-patient-specific compounded **deoxy-d-glucose** in your practice location?

This question was not displayed to the respondent.

Q453. In what practice location(s) do you stock non-patient-specific compounded **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q454. How do you obtain your stock of non-patient-specific compounded **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q455. Why do you keep a stock of non-patient-specific compounded **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q456. For which, if any, diseases or conditions do you consider **deoxy-d-glucose** standard therapy?

This question was not displayed to the respondent.

Q457. Does your specialty describe the use of **deoxy-d-glucose** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q458. What type(s) of product(s) do you use, prescribe, or recommend for **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q459. Please list any conditions or diseases for which you use compounded **diiodohydroxyquinoline** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q460.
Do you use compounded **diiodohydroxyquinoline** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q461. In which combination(s) do you use compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q462. For which, if any, diseases or conditions do you consider compounded **diiodohydroxyquinoline** standard therapy?

This question was not displayed to the respondent.

Q463. Does your specialty describe the use of compounded **diiodohydroxyquinoline** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q464. Over the past 5 years, has the frequency in which you have used compounded **diiodohydroxyquinoline** changed?

This question was not displayed to the respondent.

Q465. Why do you use compounded **diiodohydroxyquinoline** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q466. Do you stock non-patient-specific compounded **diiodohydroxyquinoline** in your practice location?

This question was not displayed to the respondent.

Q467. In what practice location(s) do you stock non-patient-specific compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q468. How do you obtain your stock of non-patient-specific compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q469. Why do you keep a stock of non-patient-specific compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q470. For which, if any, diseases or conditions do you consider **diiodohydroxyquinoline** standard therapy?

This question was not displayed to the respondent.

Q471. Does your specialty describe the use of **diiodohydroxyquinoline** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q472. What type(s) of product(s) do you use, prescribe, or recommend for **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q473. Please list any conditions or diseases for which you use compounded **diphenylcyclopropenone (DPCP)** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q474.
Do you use compounded **diphenylcyclopropenone (DPCP)** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q475. Please list all combination products in which you use compounded **diphenylcyclopropenone (DPCP)**.

This question was not displayed to the respondent.

Q476. For which, if any, diseases or conditions do you consider compounded **diphenylcyclopropenone (DPCP)** standard therapy?

This question was not displayed to the respondent.

Q477. Does your specialty describe the use of compounded **diphenylcyclopropenone (DPCP)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q478. Over the past 5 years, has the frequency in which you have used compounded **diphenylcyclopropenone (DPCP)** changed?

This question was not displayed to the respondent.

Q479. Why do you use compounded **diphenylcyclopropenone (DPCP)** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q480. Do you stock non-patient-specific compounded **diphenylcyclopropenone (DPCP)** in your practice location?

This question was not displayed to the respondent.

Q481. In what practice location(s) do you stock non-patient-specific compounded **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q482. How do you obtain your stock of non-patient-specific compounded **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q483. Why do you keep a stock of non-patient-specific compounded **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q484. For which, if any, diseases or conditions do you consider **diphenylcyclopropenone (DPCP)** standard therapy?

This question was not displayed to the respondent.

Q485. Does your specialty describe the use of **diphenylcyclopropenone (DPCP)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q486. What type(s) of product(s) do you use, prescribe, or recommend for **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q487. Please list any conditions or diseases for which you use compounded **podophyllum** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q488.
Do you use compounded **podophyllum** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q489. In which combination(s) do you use compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q490. For which, if any, diseases or conditions do you consider compounded **podophyllum** standard therapy?

This question was not displayed to the respondent.

Q491. Does your specialty describe the use of compounded **podophyllum** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q492. Over the past 5 years, has the frequency in which you have used compounded **podophyllum** changed?

This question was not displayed to the respondent.

Q493. Why do you use compounded **podophyllum** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q494. Do you stock non-patient-specific compounded **podophyllum** in your practice location?

This question was not displayed to the respondent.

Q495. In what practice location(s) do you stock non-patient-specific compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q496. How do you obtain your stock of non-patient-specific compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q497. Why do you keep a stock of non-patient-specific compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q498. For which, if any, diseases or conditions do you consider **podophyllum** standard therapy?

This question was not displayed to the respondent.

Q499. Does your specialty describe the use of **podophyllum** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q500. What type(s) of product(s) do you use, prescribe, or recommend for **podophyllum resin**? Please check all that apply.

- [ ] Compounded drug product
- [x] FDA-approved drug product
- [ ] Over the counter drug product
- [ ] Dietary supplement (e.g. vitamin or herbal supplement products sold in retail setting)
- [ ] Unsure

Q501. Please list any conditions or diseases for which you use compounded **podophyllum resin** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q502.
Do you use compounded **podophyllum resin** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q503. In which combination(s) do you use compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q504. For which, if any, diseases or conditions do you consider compounded **podophyllum resin** standard therapy?

This question was not displayed to the respondent.

Q505. Does your specialty describe the use of compounded **podophyllum resin** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q506. Over the past 5 years, has the frequency in which you have used compounded **podophyllum resin** changed?

This question was not displayed to the respondent.

Q507. Why do you use compounded **podophyllum resin** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q508. Do you stock non-patient-specific compounded **podophyllum resin** in your practice location?

This question was not displayed to the respondent.

Q509. In what practice location(s) do you stock non-patient-specific compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q510. How do you obtain your stock of non-patient-specific compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q511. Why do you keep a stock of non-patient-specific compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q512. For which, if any, diseases or conditions do you consider **podophyllum resin** standard therapy?

Condyloma acuminata

Q513. Does your specialty describe the use of **podophyllum resin** in medical practice guidelines or other resources?

Yes

Q529. What type(s) of product(s) do you use, prescribe, or recommend for **quinacrine**? Please check all that apply.

- [x] Compounded drug product
- [ ] FDA-approved drug product
- [ ] Over the counter drug product
- [ ] Dietary supplement (e.g. vitamin or herbal supplement products sold in retail setting)
- [ ] Unsure

Q530. Please list any conditions or diseases for which you use compounded **quinacrine** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

	Strength(s) (please include units)	Dosing frequency(ies)	Dosage form(s)	Route(s) of administration	Duration of therapy	Patient population
Condition 1 (please describe): Lupus vulgaris	100mg	qd	tablet	po	indef	Adult
Condition 2 (please describe)						
Condition 3 (please describe)						
Condition 4 (please describe)						
Condition 5 (please describe)						
Condition 6 (please describe)						

Condition 7 (please describe)

Condition 8 (please describe)

Q531.
Do you use compounded **quinacrine** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

- [x] Single
- [ ] Combination

Q532. Please list all combination products in which you use compounded **quinacrine**.

This question was not displayed to the respondent.

Q533. For which, if any, diseases or conditions do you consider compounded **quinacrine** standard therapy?

None (adjunct to hydroxychloroquine in recalcitrant cutaneous lupus)

Q534. Does your specialty describe the use of compounded **quinacrine** in medical practice guidelines or other resources?

Yes

Q535. Over the past 5 years, has the frequency in which you have used compounded **quinacrine** changed?

- ○ Yes - I use it **MORE** often now (briefly describe why)
- ◉ Yes - I use it **LESS** often now (briefly describe why) Shortage / unavailability
- ○ No - use has remained consistent

Q536. Why do you use compounded **quinacrine** instead of any FDA-approved drug product?

Only available via compounding.

Q537. Do you stock non-patient-specific compounded **quinacrine** in your practice location?

- ○ Yes
- ◉ No

Q538. In what practice location(s) do you stock non-patient-specific compounded **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q539. How do you obtain your stock of non-patient-specific compounded **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q540. Why do you keep a stock of non-patient-specific compounded **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q541. For which, if any, diseases or conditions do you consider **quinacrine** standard therapy?

This question was not displayed to the respondent.

Q542. Does your specialty describe the use of **quinacrine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q543. What type(s) of product(s) do you use, prescribe, or recommend for **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

- [x] Compounded drug product
- [ ] FDA-approved drug product
- [ ] Over the counter drug product
- [ ] Dietary supplement (e.g. vitamin or herbal supplement products sold in retail setting)
- [ ] Unsure

Q544. Please list any conditions or diseases for which you use compounded **squaric acid dibutyl ester (SADBE)** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

	Strength(s) (please include units)	Dosing frequency(ies)	Dosage form(s)	Route(s) of administration	Duration of therapy	Patient population
Condition 1 (please describe): Alopecia areata	2%, 0.0001%	qwk	acetone based solution	topical	Regrowth of hair	All
Condition 2 (please describe): Verruca plana / vulgaris	2%, 0.2%	tiw	acetone based solution	topical	clearance	All

Condition 3 (please describe)

Condition 4 (please describe)

Condition 5 (please describe)

Condition 6 (please describe)

Condition 7 (please describe)

Condition 8 (please describe)

Q545.
Do you use compounded **squaric acid dibutyl ester (SADBE)** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

- [x] Single
- [ ] Combination

Q546. Please list all combination products in which you use compounded **squaric acid dibutyl ester (SADBE)**.

This question was not displayed to the respondent.

Q547. For which, if any, diseases or conditions do you consider compounded **squaric acid dibutyl ester (SADBE)** standard therapy?

Alopecia areata

Q548. Does your specialty describe the use of compounded **squaric acid dibutyl ester (SADBE)** in medical practice guidelines or other resources?

Yes

Q549. Over the past 5 years, has the frequency in which you have used compounded **squaric acid dibutyl ester (SADBE)** changed?

- ○ Yes - I use it **MORE** often now (briefly describe why)
- ○ Yes - I use it **LESS** often now (briefly describe why)
- ◉ No - use has remained consistent

Q550. Why do you use compounded **squaric acid dibutyl ester (SADBE)** instead of any FDA-approved drug product?

Only available compounded

Q551. Do you stock non-patient-specific compounded **squaric acid dibutyl ester (SADBE)** in your practice location?

- ○ Yes
- ◉ No

Q552. In what practice location(s) do you stock non-patient-specific compounded **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q553. How do you obtain your stock of non-patient-specific compounded **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q554. Why do you keep a stock of non-patient-specific compounded **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q555. For which, if any, diseases or conditions do you consider **squaric acid dibutyl ester (SADBE)** standard therapy?

This question was not displayed to the respondent.

Q556. Does your specialty describe the use of **squaric acid dibutyl ester (SADBE)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q16. What is your terminal clinical degree? Please check all that apply.

- [x] Doctor of Medicine (MD)
- [ ] Doctor of Osteopathic Medicine (DO)
- [ ] Doctor of Medicine in Dentistry (DMD/DDS)
- [ ] Naturopathic Doctor (ND)
- [ ] Nurse Practitioner (NP)
- [ ] Physician Assistant (PA)
- [ ] Other (please describe)

Q17. Which of the following Board certification(s) do you hold? Please check all that apply.

- [ ] No Board certification
- [ ] Allergy and Immunology
- [ ] Anesthesiology
- [ ] Cardiovascular Disease
- [ ] Critical Care Medicine
- [x] Dermatology
- [ ] Emergency Medicine
- [ ] Endocrinology, Diabetes and Metabolism
- [ ] Family Medicine
- [ ] Gastroenterology
- [ ] Hematology
- [ ] Infectious Disease
- [ ] Internal Medicine
- [ ] Medical Toxicology
- [ ] Naturopathic Doctor
- [ ] Naturopathic Physician
- [ ] Nephrology
- [ ] Neurology
- [ ] Obstetrics and Gynecology
- [ ] Oncology
- [ ] Ophthalmology
- [ ] Otolaryngology
- [ ] Pain Medicine
- [ ] Pediatrics
- [ ] Psychiatry
- [ ] Rheumatology
- [ ] Sleep Medicine
- [ ] Surgery (please describe)
- [ ] Urology
- [ ] Other (please describe)

Q144.
The University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI), in collaboration with the Food and Drug Administration (FDA), is conducting research regarding the use of certain bulk drug substances nominated for use in compounding by outsourcing facilities under section 503B of the Federal Food, Drug, and Cosmetic Act. In particular, we are interested in the current and historic use of these substances in clinical practice.

There are **twelve (12)** substances contained in this survey. As a medical expert, we appreciate your input regarding the use of these substances in your clinical practice. This information will assist FDA in its development of a list of bulk drug substances that outsourcing facilities can use in compounding under section 503B of the Act. All responses are anonymous.

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

The time required to complete this information collection is estimated to average 30 minutes, including the time to review instructions, search existing data sources, gather the data needed, and complete and review the information collection. 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.

If you have additional questions or concerns about this research 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.

Q1. Which of the following substances do you use in your practice? Please check all that apply.

- [ ] Amphotericin B
- [ ] Boric acid
- [ ] Cantharidin
- [ ] Ciclopirox olamine
- [ ] Clioquinol
- [x] Deoxy-d-glucose
- [ ] Diiodohydroxyquinoline
- [ ] Diphenylcyclopropenone (DPCP)
- [ ] Podophyllum
- [ ] Podophyllum resin
- [ ] Quinacrine
- [ ] Squaric acid dibutyl ester (SADBE)
- [ ] None of the above

Q2. What type(s) of product(s) do you use, prescribe, or recommend for **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q3. Please list any conditions or diseases for which you use compounded **amphotericin B** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q4.

Do you use compounded **amphotericin B** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q5. Please list all combination products in which you use compounded **amphotericin B**.

This question was not displayed to the respondent.

Q6. For which, if any, diseases or conditions do you consider compounded **amphotericin B** standard therapy?

This question was not displayed to the respondent.

Q7. Does your specialty describe the use of compounded **amphotericin B** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q8. Over the past 5 years, has the frequency in which you have used compounded **amphotericin B** changed?

This question was not displayed to the respondent.

Q9. Why do you use compounded **amphotericin B** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q10. Do you stock non-patient-specific compounded **amphotericin B** in your practice location?

This question was not displayed to the respondent.

Q11. In what practice location(s) do you stock non-patient-specific compounded **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q12. How do you obtain your stock of non-patient-specific compounded **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q13. Why do you keep a stock of non-patient-specific compounded **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q14. For which, if any, diseases or conditions do you consider **amphotericin B** standard therapy?

This question was not displayed to the respondent.

Q15. Does your specialty describe the use of **amphotericin B** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q388. What type(s) of product(s) do you use, prescribe, or recommend for **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q389. Please list any conditions or diseases for which you use compounded **boric acid** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q390.
Do you use compounded **boric acid** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q391. Please list all combination products in which you use compounded **boric acid**.

This question was not displayed to the respondent.

Q392. For which, if any, diseases or conditions do you consider compounded **boric acid** standard therapy?

This question was not displayed to the respondent.

Q393. Does your specialty describe the use of compounded **boric acid** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q394. Over the past 5 years, has the frequency in which you have used compounded **boric acid** changed?

This question was not displayed to the respondent.

Q395. Why do you use compounded **boric acid** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q396. Do you stock non-patient-specific compounded **boric acid** in your practice location?

This question was not displayed to the respondent.

Q397. In what practice location(s) do you stock non-patient-specific compounded **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q398. How do you obtain your stock of non-patient-specific compounded **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q399. Why do you keep a stock of non-patient-specific compounded **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q400. For which, if any, diseases or conditions do you consider **boric acid** standard therapy?

This question was not displayed to the respondent.

Q401. Does your specialty describe the use of **boric acid** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q402. What type(s) of product(s) do you use, prescribe, or recommend for **cantharidin**? Please check all that apply.

This question was not displayed to the respondent.

Q403. Please list any conditions or diseases for which you use compounded **cantharidin** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q404.
Do you use compounded **cantharidin** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q405. In which combination(s) do you use compounded **cantharidin**? Please check all that apply.

This question was not displayed to the respondent.

Q406. For which, if any, diseases or conditions do you consider compounded **cantharidin** standard therapy?

This question was not displayed to the respondent.

Q407. Does your specialty describe the use of compounded **cantharidin** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q408. Over the past 5 years, has the frequency in which you have used compounded **cantharidin** changed?

This question was not displayed to the respondent.

Q409. Why do you use compounded **cantharidin** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q410. Do you stock non-patient-specific compounded **cantharidin** in your practice location?

This question was not displayed to the respondent.

Q411. In what practice location(s) do you stock non-patient-specific compounded **cantharidin**? Please check all that apply.

This question was not displayed to the respondent.

Q412. How do you obtain your stock of non-patient-specific compounded **cantharidin**? Please check all that apply.

This question was not displayed to the respondent.

Q413. Why do you keep a stock of non-patient-specific compounded **cantharidin**? Please check all that apply.

This question was not displayed to the respondent.

Q414. For which, if any, diseases or conditions do you consider **cantharidin** standard therapy?

This question was not displayed to the respondent.

Q415. Does your specialty describe the use of **cantharidin** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q416. What type(s) of product(s) do you use, prescribe, or recommend for **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q417. Please list any conditions or diseases for which you use compounded **ciclopirox olamine** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q418.
Do you use compounded **ciclopirox olamine** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q419. In which combination(s) do you use compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q420. For which, if any, diseases or conditions do you consider compounded **ciclopirox olamine** standard therapy?

This question was not displayed to the respondent.

Q421. Does your specialty describe the use of compounded **ciclopirox olamine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q422. Over the past 5 years, has the frequency in which you have used compounded **ciclopirox olamine** changed?

This question was not displayed to the respondent.

Q423. Why do you use compounded **ciclopirox olamine** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q424. Do you stock non-patient-specific compounded **ciclopirox olamine** in your practice location?

This question was not displayed to the respondent.

Q425. In what practice location(s) do you stock non-patient-specific compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q426. How do you obtain your stock of non-patient-specific compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q427. Why do you keep a stock of non-patient-specific compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q428. For which, if any, diseases or conditions do you consider **ciclopirox olamine** standard therapy?

This question was not displayed to the respondent.

Q429. Does your specialty describe the use of **ciclopirox olamine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q430. What type(s) of product(s) do you use, prescribe, or recommend for **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q431. Please list any conditions or diseases for which you use compounded **clioquinol** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q432.
Do you use compounded **clioquinol** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q433. In which combination(s) do you use compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q434. For which, if any, diseases or conditions do you consider compounded **clioquinol** standard therapy?

This question was not displayed to the respondent.

Q435. Does your specialty describe the use of compounded **clioquinol** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q436. Over the past 5 years, has the frequency in which you have used compounded **clioquinol** changed?

This question was not displayed to the respondent.

Q437. Why do you use compounded **clioquinol** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q438. Do you stock non-patient-specific compounded **clioquinol** in your practice location?

This question was not displayed to the respondent.

Q439. In what practice location(s) do you stock non-patient-specific compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q440. How do you obtain your stock of non-patient-specific compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q441. Why do you keep a stock of non-patient-specific compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q442. For which, if any, diseases or conditions do you consider **clioquinol** standard therapy?

This question was not displayed to the respondent.

Q443. Does your specialty describe the use of **clioquinol** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q444. What type(s) of product(s) do you use, prescribe, or recommend for **deoxy-d-glucose**? Please check all that apply.

- [x] Compounded drug product
- [ ] FDA-approved drug product

- [ ] Over the counter drug product
- [ ] Dietary supplement (e.g. vitamin or herbal supplement products sold in retail setting)
- [ ] Unsure

Q445. Please list any conditions or diseases for which you use compounded **deoxy-d-glucose** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

	Strength(s) (please include units)	Dosing frequency(ies)	Dosage form(s)	Route(s) of administration	Duration of therapy	Patient population
Condition 1 (please describe)						
Condition 2 (please describe)						
Condition 3 (please describe)						
Condition 4 (please describe)						
Condition 5 (please describe)						

Q446.
Do you use compounded **deoxy-d-glucose** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

- [ ] Single
- [x] Combination

Q447. In which combination(s) do you use compounded **deoxy-d-glucose**? Please check all that apply.

- [ ] Deoxy-d-glucose 0.2% / Acyclovir 3% / Lidocaine 1%

- [ ] Deoxy-d-glucose 0.2% / Cimetidine 10% / Ibuprofen 2% / Lidocaine 5% / Salicylic acid 15%
- [ ] Other (please describe)

Q448. For which, if any, diseases or conditions do you consider compounded **deoxy-d-glucose** standard therapy?

Q449. Does your specialty describe the use of compounded **deoxy-d-glucose** in medical practice guidelines or other resources?

Q450. Over the past 5 years, has the frequency in which you have used compounded **deoxy-d-glucose** changed?

- ( ) Yes - I use it **MORE** often now (briefly describe why)
- ( ) Yes - I use it **LESS** often now (briefly describe why)
- (•) No - use has remained consistent

Q451. Why do you use compounded **deoxy-d-glucose** instead of any FDA-approved drug product?

0

Q452. Do you stock non-patient-specific compounded **deoxy-d-glucose** in your practice location?

- (•) Yes
- ( ) No

Q453. In what practice location(s) do you stock non-patient-specific compounded **deoxy-d-glucose**? Please check all that apply.

- [ ] Physician office
- [ ] Outpatient clinic
- [ ] Emergency room
- [ ] Operating room
- [ ] Inpatient ward
- [ ] Other (please describe)

Q454. How do you obtain your stock of non-patient-specific compounded **deoxy-d-glucose**? Please check all that apply.

- [ ] Purchase from a compounding pharmacy
- [ ] Purchase from an outsourcing facility

- [ ] Compound the product yourself
- [ ] Other (please describe) [ ]

Q455. Why do you keep a stock of non-patient-specific compounded **deoxy-d-glucose**? Please check all that apply.

- [ ] Convenience
- [x] Emergencies
- [ ] Other (please describe) [ ]

Q456. For which, if any, diseases or conditions do you consider **deoxy-d-glucose** standard therapy?

This question was not displayed to the respondent.

Q457. Does your specialty describe the use of **deoxy-d-glucose** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q458. What type(s) of product(s) do you use, prescribe, or recommend for **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q459. Please list any conditions or diseases for which you use compounded **diiodohydroxyquinoline** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q460.
Do you use compounded **diiodohydroxyquinoline** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q461. In which combination(s) do you use compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q462. For which, if any, diseases or conditions do you consider compounded **diiodohydroxyquinoline** standard therapy?

This question was not displayed to the respondent.

Q463. Does your specialty describe the use of compounded **diiodohydroxyquinoline** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q464. Over the past 5 years, has the frequency in which you have used compounded **diiodohydroxyquinoline** changed?

This question was not displayed to the respondent.

Q465. Why do you use compounded **diiodohydroxyquinoline** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q466. Do you stock non-patient-specific compounded **diiodohydroxyquinoline** in your practice location?

This question was not displayed to the respondent.

Q467. In what practice location(s) do you stock non-patient-specific compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q468. How do you obtain your stock of non-patient-specific compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q469. Why do you keep a stock of non-patient-specific compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q470. For which, if any, diseases or conditions do you consider **diiodohydroxyquinoline** standard therapy?

This question was not displayed to the respondent.

Q471. Does your specialty describe the use of **diiodohydroxyquinoline** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q472. What type(s) of product(s) do you use, prescribe, or recommend for **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q473. Please list any conditions or diseases for which you use compounded **diphenylcyclopropenone (DPCP)** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q474.
Do you use compounded **diphenylcyclopropenone (DPCP)** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q475. Please list all combination products in which you use compounded **diphenylcyclopropenone (DPCP)**.

This question was not displayed to the respondent.

Q476. For which, if any, diseases or conditions do you consider compounded **diphenylcyclopropenone (DPCP)** standard therapy?

This question was not displayed to the respondent.

Q477. Does your specialty describe the use of compounded **diphenylcyclopropenone (DPCP)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q478. Over the past 5 years, has the frequency in which you have used compounded **diphenylcyclopropenone (DPCP)** changed?

This question was not displayed to the respondent.

Q479. Why do you use compounded **diphenylcyclopropenone (DPCP)** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q480. Do you stock non-patient-specific compounded **diphenylcyclopropenone (DPCP)** in your practice location?

This question was not displayed to the respondent.

Q481. In what practice location(s) do you stock non-patient-specific compounded **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q482. How do you obtain your stock of non-patient-specific compounded **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q483. Why do you keep a stock of non-patient-specific compounded **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q484. For which, if any, diseases or conditions do you consider **diphenylcyclopropenone (DPCP)** standard therapy?

This question was not displayed to the respondent.

Q485. Does your specialty describe the use of **diphenylcyclopropenone (DPCP)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q486. What type(s) of product(s) do you use, prescribe, or recommend for **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q487. Please list any conditions or diseases for which you use compounded **podophyllum** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q488.
Do you use compounded **podophyllum** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q489. In which combination(s) do you use compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q490. For which, if any, diseases or conditions do you consider compounded **podophyllum** standard therapy?

This question was not displayed to the respondent.

Q491. Does your specialty describe the use of compounded **podophyllum** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q492. Over the past 5 years, has the frequency in which you have used compounded **podophyllum** changed?

This question was not displayed to the respondent.

Q493. Why do you use compounded **podophyllum** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q494. Do you stock non-patient-specific compounded **podophyllum** in your practice location?

This question was not displayed to the respondent.

Q495. In what practice location(s) do you stock non-patient-specific compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q496. How do you obtain your stock of non-patient-specific compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q497. Why do you keep a stock of non-patient-specific compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q498. For which, if any, diseases or conditions do you consider **podophyllum** standard therapy?

This question was not displayed to the respondent.

Q499. Does your specialty describe the use of **podophyllum** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q500. What type(s) of product(s) do you use, prescribe, or recommend for **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q501. Please list any conditions or diseases for which you use compounded **podophyllum resin** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q502.
Do you use compounded **podophyllum resin** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q503. In which combination(s) do you use compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q504. For which, if any, diseases or conditions do you consider compounded **podophyllum resin** standard therapy?

This question was not displayed to the respondent.

Q505. Does your specialty describe the use of compounded **podophyllum resin** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q506. Over the past 5 years, has the frequency in which you have used compounded **podophyllum resin** changed?

This question was not displayed to the respondent.

Q507. Why do you use compounded **podophyllum resin** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q508. Do you stock non-patient-specific compounded **podophyllum resin** in your practice location?

This question was not displayed to the respondent.

Q509. In what practice location(s) do you stock non-patient-specific compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q510. How do you obtain your stock of non-patient-specific compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q511. Why do you keep a stock of non-patient-specific compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q512. For which, if any, diseases or conditions do you consider **podophyllum resin** standard therapy?

This question was not displayed to the respondent.

Q513. Does your specialty describe the use of **podophyllum resin** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q529. What type(s) of product(s) do you use, prescribe, or recommend for **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q530. Please list any conditions or diseases for which you use compounded **quinacrine** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q531.
Do you use compounded **quinacrine** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q532. Please list all combination products in which you use compounded **quinacrine**.

This question was not displayed to the respondent.

Q533. For which, if any, diseases or conditions do you consider compounded **quinacrine** standard therapy?

This question was not displayed to the respondent.

Q534. Does your specialty describe the use of compounded **quinacrine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q535. Over the past 5 years, has the frequency in which you have used compounded **quinacrine** changed?

This question was not displayed to the respondent.

Q536. Why do you use compounded **quinacrine** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q537. Do you stock non-patient-specific compounded **quinacrine** in your practice location?

This question was not displayed to the respondent.

Q538. In what practice location(s) do you stock non-patient-specific compounded **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q539. How do you obtain your stock of non-patient-specific compounded **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q540. Why do you keep a stock of non-patient-specific compounded **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q541. For which, if any, diseases or conditions do you consider **quinacrine** standard therapy?

This question was not displayed to the respondent.

Q542. Does your specialty describe the use of **quinacrine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q543. What type(s) of product(s) do you use, prescribe, or recommend for **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q544. Please list any conditions or diseases for which you use compounded **squaric acid dibutyl ester (SADBE)** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q545.
Do you use compounded **squaric acid dibutyl ester (SADBE)** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q546. Please list all combination products in which you use compounded **squaric acid dibutyl ester (SADBE)**.

This question was not displayed to the respondent.

Q547. For which, if any, diseases or conditions do you consider compounded **squaric acid dibutyl ester (SADBE)** standard therapy?

This question was not displayed to the respondent.

Q548. Does your specialty describe the use of compounded **squaric acid dibutyl ester (SADBE)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q549. Over the past 5 years, has the frequency in which you have used compounded **squaric acid dibutyl ester (SADBE)** changed?

This question was not displayed to the respondent.

Q550. Why do you use compounded **squaric acid dibutyl ester (SADBE)** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q551. Do you stock non-patient-specific compounded **squaric acid dibutyl ester (SADBE)** in your practice location?

This question was not displayed to the respondent.

Q552. In what practice location(s) do you stock non-patient-specific compounded **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q553. How do you obtain your stock of non-patient-specific compounded **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q554. Why do you keep a stock of non-patient-specific compounded **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q555. For which, if any, diseases or conditions do you consider **squaric acid dibutyl ester (SADBE)** standard therapy?

This question was not displayed to the respondent.

Q556. Does your specialty describe the use of **squaric acid dibutyl ester (SADBE)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q16. What is your terminal clinical degree? Please check all that apply.

This question was not displayed to the respondent.

Q17. Which of the following Board certification(s) do you hold? Please check all that apply.

This question was not displayed to the respondent.

Q144.
The University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI), in collaboration with the Food and Drug Administration (FDA), is conducting research regarding the use of certain bulk drug substances nominated for use in compounding by outsourcing facilities under section 503B of the Federal Food, Drug, and Cosmetic Act. In particular, we are interested in the current and historic use of these substances in clinical practice.

There are **twelve (12)** substances contained in this survey. As a medical expert, we appreciate your input regarding the use of these substances in your clinical practice. This information will assist FDA in its development of a list of bulk drug substances that outsourcing facilities can use in compounding under section 503B of the Act. All responses are anonymous.

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

The time required to complete this information collection is estimated to average 30 minutes, including the time to review instructions, search existing data sources, gather the data needed, and complete and review the information collection. 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.

If you have additional questions or concerns about this research 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.

Q1. Which of the following substances do you use in your practice? Please check all that apply.

- [ ] Amphotericin B
- [ ] Boric acid
- [x] Cantharidin
- [ ] Ciclopirox olamine
- [ ] Clioquinol
- [ ] Deoxy-d-glucose
- [ ] Diiodohydroxyquinoline
- [x] Diphenylcyclopropenone (DPCP)
- [ ] Podophyllum
- [ ] Podophyllum resin
- [ ] Quinacrine
- [x] Squaric acid dibutyl ester (SADBE)
- [ ] None of the above

Q2. What type(s) of product(s) do you use, prescribe, or recommend for **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q3. Please list any conditions or diseases for which you use compounded **amphotericin B** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q4.

Do you use compounded **amphotericin B** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q5. Please list all combination products in which you use compounded **amphotericin B**.

This question was not displayed to the respondent.

Q6. For which, if any, diseases or conditions do you consider compounded **amphotericin B** standard therapy?

This question was not displayed to the respondent.

Q7. Does your specialty describe the use of compounded **amphotericin B** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q8. Over the past 5 years, has the frequency in which you have used compounded **amphotericin B** changed?

This question was not displayed to the respondent.

Q9. Why do you use compounded **amphotericin B** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q10. Do you stock non-patient-specific compounded **amphotericin B** in your practice location?

This question was not displayed to the respondent.

Q11. In what practice location(s) do you stock non-patient-specific compounded **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q12. How do you obtain your stock of non-patient-specific compounded **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q13. Why do you keep a stock of non-patient-specific compounded **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q14. For which, if any, diseases or conditions do you consider **amphotericin B** standard therapy?

This question was not displayed to the respondent.

Q15. Does your specialty describe the use of **amphotericin B** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q388. What type(s) of product(s) do you use, prescribe, or recommend for **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q389. Please list any conditions or diseases for which you use compounded **boric acid** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q390.
Do you use compounded **boric acid** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q391. Please list all combination products in which you use compounded **boric acid**.

This question was not displayed to the respondent.

Q392. For which, if any, diseases or conditions do you consider compounded **boric acid** standard therapy?

This question was not displayed to the respondent.

Q393. Does your specialty describe the use of compounded **boric acid** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q394. Over the past 5 years, has the frequency in which you have used compounded **boric acid** changed?

This question was not displayed to the respondent.

Q395. Why do you use compounded **boric acid** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q396. Do you stock non-patient-specific compounded **boric acid** in your practice location?

This question was not displayed to the respondent.

Q397. In what practice location(s) do you stock non-patient-specific compounded **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q398. How do you obtain your stock of non-patient-specific compounded **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q399. Why do you keep a stock of non-patient-specific compounded **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q400. For which, if any, diseases or conditions do you consider **boric acid** standard therapy?

This question was not displayed to the respondent.

Q401. Does your specialty describe the use of **boric acid** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q402. What type(s) of product(s) do you use, prescribe, or recommend for **cantharidin**? Please check all that apply.

- [x] Compounded drug product
- [x] FDA-approved drug product
- [ ] Over the counter drug product
- [ ] Dietary supplement (e.g. vitamin or herbal supplement products sold in retail setting)
- [ ] Unsure

Q403. Please list any conditions or diseases for which you use compounded **cantharidin** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

	Strength(s) (please include units)	Dosing frequency(ies)	Dosage form(s)	Route(s) of administration	Duration of therapy	Patient population
Condition 1 (please describe): Molluscum			Colloid, solution	Topical		
Condition 2 (please describe): Warts						
Condition 3 (please describe)						
Condition 4 (please describe)						

Condition 5 (please describe)

Condition 6 (please describe)

Condition 7 (please describe)

Condition 8 (please describe)

Q404.
Do you use compounded **cantharidin** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

- [x] Single
- [x] Combination

Q405. In which combination(s) do you use compounded **cantharidin**? Please check all that apply.

- [ ] Cantharidin 1% / Podophyllum resin 5% / Salicylic acid 30%
- [x] Other (please describe) Cantharidin/ salicylic acid

Q406. For which, if any, diseases or conditions do you consider compounded **cantharidin** standard therapy?

Molluscum, warts

Q407. Does your specialty describe the use of compounded **cantharidin** in medical practice guidelines or other resources?

Many journal articles, texts

Q408. Over the past 5 years, has the frequency in which you have used compounded **cantharidin** changed?

- ○ Yes - I use it **MORE** often now (briefly describe why)
- ◉ Yes - I use it **LESS** often now (briefly describe why) Compounding shortage
- ○ No - use has remained consistent

Q409. Why do you use compounded **cantharidin** instead of any FDA-approved drug product?

No FDA approved treatment

Q410. Do you stock non-patient-specific compounded **cantharidin** in your practice location?

- ◉ Yes
- ○ No

Q411. In what practice location(s) do you stock non-patient-specific compounded **cantharidin**? Please check all that apply.

- ☑ Physician office
- ☐ Outpatient clinic
- ☐ Emergency room
- ☐ Operating room
- ☐ Inpatient ward
- ☐ Other (please describe)

Q412. How do you obtain your stock of non-patient-specific compounded **cantharidin**? Please check all that apply.

- ☑ Purchase from a compounding pharmacy
- ☐ Purchase from an outsourcing facility
- ☐ Compound the product yourself
- ☐ Other (please describe)

Q413. Why do you keep a stock of non-patient-specific compounded **cantharidin**? Please check all that apply.

- ☑ Convenience
- ☐ Emergencies
- ☐ Other (please describe)

Q414. For which, if any, diseases or conditions do you consider **cantharidin** standard therapy?

This question was not displayed to the respondent.

Q415. Does your specialty describe the use of **cantharidin** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q416. What type(s) of product(s) do you use, prescribe, or recommend for **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q417. Please list any conditions or diseases for which you use compounded **ciclopirox olamine** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q418.
Do you use compounded **ciclopirox olamine** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q419. In which combination(s) do you use compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q420. For which, if any, diseases or conditions do you consider compounded **ciclopirox olamine** standard therapy?

This question was not displayed to the respondent.

Q421. Does your specialty describe the use of compounded **ciclopirox olamine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q422. Over the past 5 years, has the frequency in which you have used compounded **ciclopirox olamine** changed?

This question was not displayed to the respondent.

Q423. Why do you use compounded **ciclopirox olamine** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q424. Do you stock non-patient-specific compounded **ciclopirox olamine** in your practice location?

This question was not displayed to the respondent.

Q425. In what practice location(s) do you stock non-patient-specific compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q426. How do you obtain your stock of non-patient-specific compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q427. Why do you keep a stock of non-patient-specific compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q428. For which, if any, diseases or conditions do you consider **ciclopirox olamine** standard therapy?

This question was not displayed to the respondent.

Q429. Does your specialty describe the use of **ciclopirox olamine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q430. What type(s) of product(s) do you use, prescribe, or recommend for **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q431. Please list any conditions or diseases for which you use compounded **clioquinol** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q432.
Do you use compounded **clioquinol** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q433. In which combination(s) do you use compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q434. For which, if any, diseases or conditions do you consider compounded **clioquinol** standard therapy?

This question was not displayed to the respondent.

Q435. Does your specialty describe the use of compounded **clioquinol** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q436. Over the past 5 years, has the frequency in which you have used compounded **clioquinol** changed?

This question was not displayed to the respondent.

Q437. Why do you use compounded **clioquinol** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q438. Do you stock non-patient-specific compounded **clioquinol** in your practice location?

This question was not displayed to the respondent.

Q439. In what practice location(s) do you stock non-patient-specific compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q440. How do you obtain your stock of non-patient-specific compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q441. Why do you keep a stock of non-patient-specific compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q442. For which, if any, diseases or conditions do you consider **clioquinol** standard therapy?

This question was not displayed to the respondent.

Q443. Does your specialty describe the use of **clioquinol** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q444. What type(s) of product(s) do you use, prescribe, or recommend for **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q445. Please list any conditions or diseases for which you use compounded **deoxy-d-glucose** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q446.
Do you use compounded **deoxy-d-glucose** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q447. In which combination(s) do you use compounded **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q448. For which, if any, diseases or conditions do you consider compounded **deoxy-d-glucose** standard therapy?

This question was not displayed to the respondent.

Q449. Does your specialty describe the use of compounded **deoxy-d-glucose** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q450. Over the past 5 years, has the frequency in which you have used compounded **deoxy-d-glucose** changed?

This question was not displayed to the respondent.

Q451. Why do you use compounded **deoxy-d-glucose** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q452. Do you stock non-patient-specific compounded **deoxy-d-glucose** in your practice location?

This question was not displayed to the respondent.

Q453. In what practice location(s) do you stock non-patient-specific compounded **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q454. How do you obtain your stock of non-patient-specific compounded **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q455. Why do you keep a stock of non-patient-specific compounded **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q456. For which, if any, diseases or conditions do you consider **deoxy-d-glucose** standard therapy?

This question was not displayed to the respondent.

Q457. Does your specialty describe the use of **deoxy-d-glucose** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q458. What type(s) of product(s) do you use, prescribe, or recommend for **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q459. Please list any conditions or diseases for which you use compounded **diiodohydroxyquinoline** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q460.
Do you use compounded **diiodohydroxyquinoline** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q461. In which combination(s) do you use compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q462. For which, if any, diseases or conditions do you consider compounded **diiodohydroxyquinoline** standard therapy?

This question was not displayed to the respondent.

Q463. Does your specialty describe the use of compounded **diiodohydroxyquinoline** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q464. Over the past 5 years, has the frequency in which you have used compounded **diiodohydroxyquinoline** changed?

This question was not displayed to the respondent.

Q465. Why do you use compounded **diiodohydroxyquinoline** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q466. Do you stock non-patient-specific compounded **diiodohydroxyquinoline** in your practice location?

This question was not displayed to the respondent.

Q467. In what practice location(s) do you stock non-patient-specific compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q468. How do you obtain your stock of non-patient-specific compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q469. Why do you keep a stock of non-patient-specific compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q470. For which, if any, diseases or conditions do you consider **diiodohydroxyquinoline** standard therapy?

This question was not displayed to the respondent.

Q471. Does your specialty describe the use of **diiodohydroxyquinoline** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q472. What type(s) of product(s) do you use, prescribe, or recommend for **diphenylcyclopropenone (DPCP)**? Please check all that apply.

- [x] Compounded drug product
- [x] FDA-approved drug product
- [ ] Over the counter drug product
- [ ] Dietary supplement (e.g. vitamin or herbal supplement products sold in retail setting)
- [ ] Unsure

Q473. Please list any conditions or diseases for which you use compounded **diphenylcyclopropenone (DPCP)** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q474.
Do you use compounded **diphenylcyclopropenone (DPCP)** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q475. Please list all combination products in which you use compounded **diphenylcyclopropenone (DPCP)**.

This question was not displayed to the respondent.

Q476. For which, if any, diseases or conditions do you consider compounded **diphenylcyclopropenone (DPCP)** standard therapy?

This question was not displayed to the respondent.

Q477. Does your specialty describe the use of compounded **diphenylcyclopropenone (DPCP)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q478. Over the past 5 years, has the frequency in which you have used compounded **diphenylcyclopropenone (DPCP)** changed?

This question was not displayed to the respondent.

Q479. Why do you use compounded **diphenylcyclopropenone (DPCP)** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q480. Do you stock non-patient-specific compounded **diphenylcyclopropenone (DPCP)** in your practice location?

This question was not displayed to the respondent.

Q481. In what practice location(s) do you stock non-patient-specific compounded **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q482. How do you obtain your stock of non-patient-specific compounded **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q483. Why do you keep a stock of non-patient-specific compounded **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q484. For which, if any, diseases or conditions do you consider **diphenylcyclopropenone (DPCP)** standard therapy?

This question was not displayed to the respondent.

Q485. Does your specialty describe the use of **diphenylcyclopropenone (DPCP)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q486. What type(s) of product(s) do you use, prescribe, or recommend for **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q487. Please list any conditions or diseases for which you use compounded **podophyllum** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q488.
Do you use compounded **podophyllum** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q489. In which combination(s) do you use compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q490. For which, if any, diseases or conditions do you consider compounded **podophyllum** standard therapy?

This question was not displayed to the respondent.

Q491. Does your specialty describe the use of compounded **podophyllum** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q492. Over the past 5 years, has the frequency in which you have used compounded **podophyllum** changed?

This question was not displayed to the respondent.

Q493. Why do you use compounded **podophyllum** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q494. Do you stock non-patient-specific compounded **podophyllum** in your practice location?

This question was not displayed to the respondent.

Q495. In what practice location(s) do you stock non-patient-specific compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q496. How do you obtain your stock of non-patient-specific compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q497. Why do you keep a stock of non-patient-specific compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q498. For which, if any, diseases or conditions do you consider **podophyllum** standard therapy?

This question was not displayed to the respondent.

Q499. Does your specialty describe the use of **podophyllum** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q500. What type(s) of product(s) do you use, prescribe, or recommend for **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q501. Please list any conditions or diseases for which you use compounded **podophyllum resin** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q502.
Do you use compounded **podophyllum resin** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q503. In which combination(s) do you use compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q504. For which, if any, diseases or conditions do you consider compounded **podophyllum resin** standard therapy?

This question was not displayed to the respondent.

Q505. Does your specialty describe the use of compounded **podophyllum resin** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q506. Over the past 5 years, has the frequency in which you have used compounded **podophyllum resin** changed?

This question was not displayed to the respondent.

Q507. Why do you use compounded **podophyllum resin** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q508. Do you stock non-patient-specific compounded **podophyllum resin** in your practice location?

This question was not displayed to the respondent.

Q509. In what practice location(s) do you stock non-patient-specific compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q510. How do you obtain your stock of non-patient-specific compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q511. Why do you keep a stock of non-patient-specific compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q512. For which, if any, diseases or conditions do you consider **podophyllum resin** standard therapy?

This question was not displayed to the respondent.

Q513. Does your specialty describe the use of **podophyllum resin** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q529. What type(s) of product(s) do you use, prescribe, or recommend for **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q530. Please list any conditions or diseases for which you use compounded **quinacrine** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q531.
Do you use compounded **quinacrine** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q532. Please list all combination products in which you use compounded **quinacrine**.

This question was not displayed to the respondent.

Q533. For which, if any, diseases or conditions do you consider compounded **quinacrine** standard therapy?

This question was not displayed to the respondent.

Q534. Does your specialty describe the use of compounded **quinacrine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q535. Over the past 5 years, has the frequency in which you have used compounded **quinacrine** changed?

This question was not displayed to the respondent.

Q536. Why do you use compounded **quinacrine** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q537. Do you stock non-patient-specific compounded **quinacrine** in your practice location?

This question was not displayed to the respondent.

Q538. In what practice location(s) do you stock non-patient-specific compounded **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q539. How do you obtain your stock of non-patient-specific compounded **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q540. Why do you keep a stock of non-patient-specific compounded **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q541. For which, if any, diseases or conditions do you consider **quinacrine** standard therapy?

This question was not displayed to the respondent.

Q542. Does your specialty describe the use of **quinacrine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q543. What type(s) of product(s) do you use, prescribe, or recommend for **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q544. Please list any conditions or diseases for which you use compounded **squaric acid dibutyl ester (SADBE)** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q545.
Do you use compounded **squaric acid dibutyl ester (SADBE)** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q546. Please list all combination products in which you use compounded **squaric acid dibutyl ester (SADBE)**.

This question was not displayed to the respondent.

Q547. For which, if any, diseases or conditions do you consider compounded **squaric acid dibutyl ester (SADBE)** standard therapy?

This question was not displayed to the respondent.

Q548. Does your specialty describe the use of compounded **squaric acid dibutyl ester (SADBE)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q549. Over the past 5 years, has the frequency in which you have used compounded **squaric acid dibutyl ester (SADBE)** changed?

This question was not displayed to the respondent.

Q550. Why do you use compounded **squaric acid dibutyl ester (SADBE)** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q551. Do you stock non-patient-specific compounded **squaric acid dibutyl ester (SADBE)** in your practice location?

This question was not displayed to the respondent.

Q552. In what practice location(s) do you stock non-patient-specific compounded **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q553. How do you obtain your stock of non-patient-specific compounded **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q554. Why do you keep a stock of non-patient-specific compounded **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q555. For which, if any, diseases or conditions do you consider **squaric acid dibutyl ester (SADBE)** standard therapy?

This question was not displayed to the respondent.

Q556. Does your specialty describe the use of **squaric acid dibutyl ester (SADBE)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q16. What is your terminal clinical degree? Please check all that apply.

This question was not displayed to the respondent.

Q17. Which of the following Board certification(s) do you hold? Please check all that apply.

This question was not displayed to the respondent.

Q144.
The University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI), in collaboration with the Food and Drug Administration (FDA), is conducting research regarding the use of certain bulk drug substances nominated for use in compounding by outsourcing facilities under section 503B of the Federal Food, Drug, and Cosmetic Act. In particular, we are interested in the current and historic use of these substances in clinical practice.

There are **twelve (12)** substances contained in this survey. As a medical expert, we appreciate your input regarding the use of these substances in your clinical practice. This information will assist FDA in its development of a list of bulk drug substances that outsourcing facilities can use in compounding under section 503B of the Act. All responses are anonymous.

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

The time required to complete this information collection is estimated to average 30 minutes, including the time to review instructions, search existing data sources, gather the data needed, and complete and review the information collection. 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.

If you have additional questions or concerns about this research 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.

Q1. Which of the following substances do you use in your practice? Please check all that apply.

- [ ] Amphotericin B
- [ ] Boric acid
- [x] Cantharidin
- [x] Ciclopirox olamine
- [ ] Clioquinol
- [ ] Deoxy-d-glucose
- [ ] Diiodohydroxyquinoline
- [x] Diphenylcyclopropenone (DPCP)
- [x] Podophyllum
- [x] Podophyllum resin
- [ ] Quinacrine
- [x] Squaric acid dibutyl ester (SADBE)
- [ ] None of the above

Q2. What type(s) of product(s) do you use, prescribe, or recommend for **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q3. Please list any conditions or diseases for which you use compounded **amphotericin B** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q4.
Do you use compounded **amphotericin B** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q5. Please list all combination products in which you use compounded **amphotericin B**.

This question was not displayed to the respondent.

Q6. For which, if any, diseases or conditions do you consider compounded **amphotericin B** standard therapy?

This question was not displayed to the respondent.

Q7. Does your specialty describe the use of compounded **amphotericin B** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q8. Over the past 5 years, has the frequency in which you have used compounded **amphotericin B** changed?

This question was not displayed to the respondent.

Q9. Why do you use compounded **amphotericin B** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q10. Do you stock non-patient-specific compounded **amphotericin B** in your practice location?

This question was not displayed to the respondent.

Q11. In what practice location(s) do you stock non-patient-specific compounded **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q12. How do you obtain your stock of non-patient-specific compounded **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q13. Why do you keep a stock of non-patient-specific compounded **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q14. For which, if any, diseases or conditions do you consider **amphotericin B** standard therapy?

This question was not displayed to the respondent.

Q15. Does your specialty describe the use of **amphotericin B** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q388. What type(s) of product(s) do you use, prescribe, or recommend for **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q389. Please list any conditions or diseases for which you use compounded **boric acid** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q390.
Do you use compounded **boric acid** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q391. Please list all combination products in which you use compounded **boric acid**.

This question was not displayed to the respondent.

Q392. For which, if any, diseases or conditions do you consider compounded **boric acid** standard therapy?

This question was not displayed to the respondent.

Q393. Does your specialty describe the use of compounded **boric acid** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q394. Over the past 5 years, has the frequency in which you have used compounded **boric acid** changed?

This question was not displayed to the respondent.

Q395. Why do you use compounded **boric acid** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q396. Do you stock non-patient-specific compounded **boric acid** in your practice location?

This question was not displayed to the respondent.

Q397. In what practice location(s) do you stock non-patient-specific compounded **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q398. How do you obtain your stock of non-patient-specific compounded **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q399. Why do you keep a stock of non-patient-specific compounded **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q400. For which, if any, diseases or conditions do you consider **boric acid** standard therapy?

This question was not displayed to the respondent.

Q401. Does your specialty describe the use of **boric acid** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q402. What type(s) of product(s) do you use, prescribe, or recommend for **cantharidin**? Please check all that apply.

- [x] Compounded drug product

- [ ] FDA-approved drug product
- [ ] Over the counter drug product
- [ ] Dietary supplement (e.g. vitamin or herbal supplement products sold in retail setting)
- [ ] Unsure

Q403. Please list any conditions or diseases for which you use compounded **cantharidin** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q404.
Do you use compounded **cantharidin** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q405. In which combination(s) do you use compounded **cantharidin**? Please check all that apply.

This question was not displayed to the respondent.

Q406. For which, if any, diseases or conditions do you consider compounded **cantharidin** standard therapy?

This question was not displayed to the respondent.

Q407. Does your specialty describe the use of compounded **cantharidin** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q408. Over the past 5 years, has the frequency in which you have used compounded **cantharidin** changed?

This question was not displayed to the respondent.

Q409. Why do you use compounded **cantharidin** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q410. Do you stock non-patient-specific compounded **cantharidin** in your practice location?

This question was not displayed to the respondent.

Q411. In what practice location(s) do you stock non-patient-specific compounded **cantharidin**? Please check all that apply.

This question was not displayed to the respondent.

Q412. How do you obtain your stock of non-patient-specific compounded **cantharidin**? Please check all that apply.

This question was not displayed to the respondent.

Q413. Why do you keep a stock of non-patient-specific compounded **cantharidin**? Please check all that apply.

This question was not displayed to the respondent.

Q414. For which, if any, diseases or conditions do you consider **cantharidin** standard therapy?

This question was not displayed to the respondent.

Q415. Does your specialty describe the use of **cantharidin** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q416. What type(s) of product(s) do you use, prescribe, or recommend for **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q417. Please list any conditions or diseases for which you use compounded **ciclopirox olamine** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q418.
Do you use compounded **ciclopirox olamine** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q419. In which combination(s) do you use compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q420. For which, if any, diseases or conditions do you consider compounded **ciclopirox olamine** standard therapy?

This question was not displayed to the respondent.

Q421. Does your specialty describe the use of compounded **ciclopirox olamine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q422. Over the past 5 years, has the frequency in which you have used compounded **ciclopirox olamine** changed?

This question was not displayed to the respondent.

Q423. Why do you use compounded **ciclopirox olamine** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q424. Do you stock non-patient-specific compounded **ciclopirox olamine** in your practice location?

This question was not displayed to the respondent.

Q425. In what practice location(s) do you stock non-patient-specific compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q426. How do you obtain your stock of non-patient-specific compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q427. Why do you keep a stock of non-patient-specific compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q428. For which, if any, diseases or conditions do you consider **ciclopirox olamine** standard therapy?

This question was not displayed to the respondent.

Q429. Does your specialty describe the use of **ciclopirox olamine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q430. What type(s) of product(s) do you use, prescribe, or recommend for **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q431. Please list any conditions or diseases for which you use compounded **clioquinol** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q432.
Do you use compounded **clioquinol** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q433. In which combination(s) do you use compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q434. For which, if any, diseases or conditions do you consider compounded **clioquinol** standard therapy?

This question was not displayed to the respondent.

Q435. Does your specialty describe the use of compounded **clioquinol** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q436. Over the past 5 years, has the frequency in which you have used compounded **clioquinol** changed?

This question was not displayed to the respondent.

Q437. Why do you use compounded **clioquinol** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q438. Do you stock non-patient-specific compounded **clioquinol** in your practice location?

This question was not displayed to the respondent.

Q439. In what practice location(s) do you stock non-patient-specific compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q440. How do you obtain your stock of non-patient-specific compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q441. Why do you keep a stock of non-patient-specific compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q442. For which, if any, diseases or conditions do you consider **clioquinol** standard therapy?

This question was not displayed to the respondent.

Q443. Does your specialty describe the use of **clioquinol** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q444. What type(s) of product(s) do you use, prescribe, or recommend for **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q445. Please list any conditions or diseases for which you use compounded **deoxy-d-glucose** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q446.
Do you use compounded **deoxy-d-glucose** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q447. In which combination(s) do you use compounded **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q448. For which, if any, diseases or conditions do you consider compounded **deoxy-d-glucose** standard therapy?

This question was not displayed to the respondent.

Q449. Does your specialty describe the use of compounded **deoxy-d-glucose** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q450. Over the past 5 years, has the frequency in which you have used compounded **deoxy-d-glucose** changed?

This question was not displayed to the respondent.

Q451. Why do you use compounded **deoxy-d-glucose** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q452. Do you stock non-patient-specific compounded **deoxy-d-glucose** in your practice location?

This question was not displayed to the respondent.

Q453. In what practice location(s) do you stock non-patient-specific compounded **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q454. How do you obtain your stock of non-patient-specific compounded **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q455. Why do you keep a stock of non-patient-specific compounded **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q456. For which, if any, diseases or conditions do you consider **deoxy-d-glucose** standard therapy?

This question was not displayed to the respondent.

Q457. Does your specialty describe the use of **deoxy-d-glucose** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q458. What type(s) of product(s) do you use, prescribe, or recommend for **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q459. Please list any conditions or diseases for which you use compounded **diiodohydroxyquinoline** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q460.
Do you use compounded **diiodohydroxyquinoline** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q461. In which combination(s) do you use compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q462. For which, if any, diseases or conditions do you consider compounded **diiodohydroxyquinoline** standard therapy?

This question was not displayed to the respondent.

Q463. Does your specialty describe the use of compounded **diiodohydroxyquinoline** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q464. Over the past 5 years, has the frequency in which you have used compounded **diiodohydroxyquinoline** changed?

This question was not displayed to the respondent.

Q465. Why do you use compounded **diiodohydroxyquinoline** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q466. Do you stock non-patient-specific compounded **diiodohydroxyquinoline** in your practice location?

This question was not displayed to the respondent.

Q467. In what practice location(s) do you stock non-patient-specific compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q468. How do you obtain your stock of non-patient-specific compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q469. Why do you keep a stock of non-patient-specific compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q470. For which, if any, diseases or conditions do you consider **diiodohydroxyquinoline** standard therapy?

This question was not displayed to the respondent.

Q471. Does your specialty describe the use of **diiodohydroxyquinoline** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q472. What type(s) of product(s) do you use, prescribe, or recommend for **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q473. Please list any conditions or diseases for which you use compounded **diphenylcyclopropenone (DPCP)** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q474.
Do you use compounded **diphenylcyclopropenone (DPCP)** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q475. Please list all combination products in which you use compounded **diphenylcyclopropenone (DPCP)**.

This question was not displayed to the respondent.

Q476. For which, if any, diseases or conditions do you consider compounded **diphenylcyclopropenone (DPCP)** standard therapy?

This question was not displayed to the respondent.

Q477. Does your specialty describe the use of compounded **diphenylcyclopropenone (DPCP)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q478. Over the past 5 years, has the frequency in which you have used compounded **diphenylcyclopropenone (DPCP)** changed?

This question was not displayed to the respondent.

Q479. Why do you use compounded **diphenylcyclopropenone (DPCP)** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q480. Do you stock non-patient-specific compounded **diphenylcyclopropenone (DPCP)** in your practice location?

This question was not displayed to the respondent.

Q481. In what practice location(s) do you stock non-patient-specific compounded **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q482. How do you obtain your stock of non-patient-specific compounded **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q483. Why do you keep a stock of non-patient-specific compounded **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q484. For which, if any, diseases or conditions do you consider **diphenylcyclopropenone (DPCP)** standard therapy?

This question was not displayed to the respondent.

Q485. Does your specialty describe the use of **diphenylcyclopropenone (DPCP)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q486. What type(s) of product(s) do you use, prescribe, or recommend for **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q487. Please list any conditions or diseases for which you use compounded **podophyllum** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q488.
Do you use compounded **podophyllum** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q489. In which combination(s) do you use compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q490. For which, if any, diseases or conditions do you consider compounded **podophyllum** standard therapy?

This question was not displayed to the respondent.

Q491. Does your specialty describe the use of compounded **podophyllum** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q492. Over the past 5 years, has the frequency in which you have used compounded **podophyllum** changed?

This question was not displayed to the respondent.

Q493. Why do you use compounded **podophyllum** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q494. Do you stock non-patient-specific compounded **podophyllum** in your practice location?

This question was not displayed to the respondent.

Q495. In what practice location(s) do you stock non-patient-specific compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q496. How do you obtain your stock of non-patient-specific compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q497. Why do you keep a stock of non-patient-specific compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q498. For which, if any, diseases or conditions do you consider **podophyllum** standard therapy?

This question was not displayed to the respondent.

Q499. Does your specialty describe the use of **podophyllum** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q500. What type(s) of product(s) do you use, prescribe, or recommend for **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q501. Please list any conditions or diseases for which you use compounded **podophyllum resin** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q502.
Do you use compounded **podophyllum resin** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q503. In which combination(s) do you use compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q504. For which, if any, diseases or conditions do you consider compounded **podophyllum resin** standard therapy?

This question was not displayed to the respondent.

Q505. Does your specialty describe the use of compounded **podophyllum resin** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q506. Over the past 5 years, has the frequency in which you have used compounded **podophyllum resin** changed?

This question was not displayed to the respondent.

Q507. Why do you use compounded **podophyllum resin** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q508. Do you stock non-patient-specific compounded **podophyllum resin** in your practice location?

This question was not displayed to the respondent.

Q509. In what practice location(s) do you stock non-patient-specific compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q510. How do you obtain your stock of non-patient-specific compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q511. Why do you keep a stock of non-patient-specific compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q512. For which, if any, diseases or conditions do you consider **podophyllum resin** standard therapy?

This question was not displayed to the respondent.

Q513. Does your specialty describe the use of **podophyllum resin** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q529. What type(s) of product(s) do you use, prescribe, or recommend for **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q530. Please list any conditions or diseases for which you use compounded **quinacrine** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q531.
Do you use compounded **quinacrine** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q532. Please list all combination products in which you use compounded **quinacrine**.

This question was not displayed to the respondent.

Q533. For which, if any, diseases or conditions do you consider compounded **quinacrine** standard therapy?

This question was not displayed to the respondent.

Q534. Does your specialty describe the use of compounded **quinacrine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q535. Over the past 5 years, has the frequency in which you have used compounded **quinacrine** changed?

This question was not displayed to the respondent.

Q536. Why do you use compounded **quinacrine** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q537. Do you stock non-patient-specific compounded **quinacrine** in your practice location?

This question was not displayed to the respondent.

Q538. In what practice location(s) do you stock non-patient-specific compounded **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q539. How do you obtain your stock of non-patient-specific compounded **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q540. Why do you keep a stock of non-patient-specific compounded **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q541. For which, if any, diseases or conditions do you consider **quinacrine** standard therapy?

This question was not displayed to the respondent.

Q542. Does your specialty describe the use of **quinacrine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q543. What type(s) of product(s) do you use, prescribe, or recommend for **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q544. Please list any conditions or diseases for which you use compounded **squaric acid dibutyl ester (SADBE)** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q545.
Do you use compounded **squaric acid dibutyl ester (SADBE)** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q546. Please list all combination products in which you use compounded **squaric acid dibutyl ester (SADBE)**.

This question was not displayed to the respondent.

Q547. For which, if any, diseases or conditions do you consider compounded **squaric acid dibutyl ester (SADBE)** standard therapy?

This question was not displayed to the respondent.

Q548. Does your specialty describe the use of compounded **squaric acid dibutyl ester (SADBE)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q549. Over the past 5 years, has the frequency in which you have used compounded **squaric acid dibutyl ester (SADBE)** changed?

This question was not displayed to the respondent.

Q550. Why do you use compounded **squaric acid dibutyl ester (SADBE)** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q551. Do you stock non-patient-specific compounded **squaric acid dibutyl ester (SADBE)** in your practice location?

This question was not displayed to the respondent.

Q552. In what practice location(s) do you stock non-patient-specific compounded **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q553. How do you obtain your stock of non-patient-specific compounded **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q554. Why do you keep a stock of non-patient-specific compounded **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q555. For which, if any, diseases or conditions do you consider **squaric acid dibutyl ester (SADBE)** standard therapy?

This question was not displayed to the respondent.

Q556. Does your specialty describe the use of **squaric acid dibutyl ester (SADBE)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q16. What is your terminal clinical degree? Please check all that apply.

This question was not displayed to the respondent.

Q17. Which of the following Board certification(s) do you hold? Please check all that apply.

This question was not displayed to the respondent.

Q144.
The University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI), in collaboration with the Food and Drug Administration (FDA), is conducting research regarding the use of certain bulk drug substances nominated for use in compounding by outsourcing facilities under section 503B of the Federal Food, Drug, and Cosmetic Act. In particular, we are interested in the current and historic use of these substances in clinical practice.

There are **twelve (12)** substances contained in this survey. As a medical expert, we appreciate your input regarding the use of these substances in your clinical practice. This information will assist FDA in its development of a list of bulk drug substances that outsourcing facilities can use in compounding under section 503B of the Act. All responses are anonymous.

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

The time required to complete this information collection is estimated to average 30 minutes, including the time to review instructions, search existing data sources, gather the data needed, and complete and review the information collection. 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.

If you have additional questions or concerns about this research 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.

Q1. Which of the following substances do you use in your practice? Please check all that apply.

- [ ] Amphotericin B
- [ ] Boric acid
- [ ] Cantharidin
- [ ] Ciclopirox olamine
- [ ] Clioquinol
- [ ] Deoxy-d-glucose
- [ ] Diiodohydroxyquinoline
- [ ] Diphenylcyclopropenone (DPCP)
- [ ] Podophyllum
- [ ] Podophyllum resin
- [ ] Quinacrine
- [x] Squaric acid dibutyl ester (SADBE)
- [ ] None of the above

Q2. What type(s) of product(s) do you use, prescribe, or recommend for **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q3. Please list any conditions or diseases for which you use compounded **amphotericin B** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q4.

Do you use compounded **amphotericin B** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q5. Please list all combination products in which you use compounded **amphotericin B**.

This question was not displayed to the respondent.

Q6. For which, if any, diseases or conditions do you consider compounded **amphotericin B** standard therapy?

This question was not displayed to the respondent.

Q7. Does your specialty describe the use of compounded **amphotericin B** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q8. Over the past 5 years, has the frequency in which you have used compounded **amphotericin B** changed?

This question was not displayed to the respondent.

Q9. Why do you use compounded **amphotericin B** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q10. Do you stock non-patient-specific compounded **amphotericin B** in your practice location?

This question was not displayed to the respondent.

Q11. In what practice location(s) do you stock non-patient-specific compounded **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q12. How do you obtain your stock of non-patient-specific compounded **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q13. Why do you keep a stock of non-patient-specific compounded **amphotericin B**? Please check all that apply.

This question was not displayed to the respondent.

Q14. For which, if any, diseases or conditions do you consider **amphotericin B** standard therapy?

This question was not displayed to the respondent.

Q15. Does your specialty describe the use of **amphotericin B** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q388. What type(s) of product(s) do you use, prescribe, or recommend for **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q389. Please list any conditions or diseases for which you use compounded **boric acid** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q390.
Do you use compounded **boric acid** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q391. Please list all combination products in which you use compounded **boric acid**.

This question was not displayed to the respondent.

Q392. For which, if any, diseases or conditions do you consider compounded **boric acid** standard therapy?

This question was not displayed to the respondent.

Q393. Does your specialty describe the use of compounded **boric acid** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q394. Over the past 5 years, has the frequency in which you have used compounded **boric acid** changed?

This question was not displayed to the respondent.

Q395. Why do you use compounded **boric acid** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q396. Do you stock non-patient-specific compounded **boric acid** in your practice location?

This question was not displayed to the respondent.

Q397. In what practice location(s) do you stock non-patient-specific compounded **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q398. How do you obtain your stock of non-patient-specific compounded **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q399. Why do you keep a stock of non-patient-specific compounded **boric acid**? Please check all that apply.

This question was not displayed to the respondent.

Q400. For which, if any, diseases or conditions do you consider **boric acid** standard therapy?

This question was not displayed to the respondent.

Q401. Does your specialty describe the use of **boric acid** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q402. What type(s) of product(s) do you use, prescribe, or recommend for **cantharidin**? Please check all that apply.

This question was not displayed to the respondent.

Q403. Please list any conditions or diseases for which you use compounded **cantharidin** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q404.
Do you use compounded **cantharidin** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q405. In which combination(s) do you use compounded **cantharidin**? Please check all that apply.

This question was not displayed to the respondent.

Q406. For which, if any, diseases or conditions do you consider compounded **cantharidin** standard therapy?

This question was not displayed to the respondent.

Q407. Does your specialty describe the use of compounded **cantharidin** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q408. Over the past 5 years, has the frequency in which you have used compounded **cantharidin** changed?

This question was not displayed to the respondent.

Q409. Why do you use compounded **cantharidin** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q410. Do you stock non-patient-specific compounded **cantharidin** in your practice location?

This question was not displayed to the respondent.

Q411. In what practice location(s) do you stock non-patient-specific compounded **cantharidin**? Please check all that apply.

This question was not displayed to the respondent.

Q412. How do you obtain your stock of non-patient-specific compounded **cantharidin**? Please check all that apply.

This question was not displayed to the respondent.

Q413. Why do you keep a stock of non-patient-specific compounded **cantharidin**? Please check all that apply.

This question was not displayed to the respondent.

Q414. For which, if any, diseases or conditions do you consider **cantharidin** standard therapy?

This question was not displayed to the respondent.

Q415. Does your specialty describe the use of **cantharidin** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q416. What type(s) of product(s) do you use, prescribe, or recommend for **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q417. Please list any conditions or diseases for which you use compounded **ciclopirox olamine** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q418.
Do you use compounded **ciclopirox olamine** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q419. In which combination(s) do you use compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q420. For which, if any, diseases or conditions do you consider compounded **ciclopirox olamine** standard therapy?

This question was not displayed to the respondent.

Q421. Does your specialty describe the use of compounded **ciclopirox olamine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q422. Over the past 5 years, has the frequency in which you have used compounded **ciclopirox olamine** changed?

This question was not displayed to the respondent.

Q423. Why do you use compounded **ciclopirox olamine** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q424. Do you stock non-patient-specific compounded **ciclopirox olamine** in your practice location?

This question was not displayed to the respondent.

Q425. In what practice location(s) do you stock non-patient-specific compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q426. How do you obtain your stock of non-patient-specific compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q427. Why do you keep a stock of non-patient-specific compounded **ciclopirox olamine**? Please check all that apply.

This question was not displayed to the respondent.

Q428. For which, if any, diseases or conditions do you consider **ciclopirox olamine** standard therapy?

This question was not displayed to the respondent.

Q429. Does your specialty describe the use of **ciclopirox olamine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q430. What type(s) of product(s) do you use, prescribe, or recommend for **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q431. Please list any conditions or diseases for which you use compounded **clioquinol** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q432.
Do you use compounded **clioquinol** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q433. In which combination(s) do you use compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q434. For which, if any, diseases or conditions do you consider compounded **clioquinol** standard therapy?

This question was not displayed to the respondent.

Q435. Does your specialty describe the use of compounded **clioquinol** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q436. Over the past 5 years, has the frequency in which you have used compounded **clioquinol** changed?

This question was not displayed to the respondent.

Q437. Why do you use compounded **clioquinol** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q438. Do you stock non-patient-specific compounded **clioquinol** in your practice location?

This question was not displayed to the respondent.

Q439. In what practice location(s) do you stock non-patient-specific compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q440. How do you obtain your stock of non-patient-specific compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q441. Why do you keep a stock of non-patient-specific compounded **clioquinol**? Please check all that apply.

This question was not displayed to the respondent.

Q442. For which, if any, diseases or conditions do you consider **clioquinol** standard therapy?

This question was not displayed to the respondent.

Q443. Does your specialty describe the use of **clioquinol** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q444. What type(s) of product(s) do you use, prescribe, or recommend for **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q445. Please list any conditions or diseases for which you use compounded **deoxy-d-glucose** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q446.
Do you use compounded **deoxy-d-glucose** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q447. In which combination(s) do you use compounded **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q448. For which, if any, diseases or conditions do you consider compounded **deoxy-d-glucose** standard therapy?

This question was not displayed to the respondent.

Q449. Does your specialty describe the use of compounded **deoxy-d-glucose** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q450. Over the past 5 years, has the frequency in which you have used compounded **deoxy-d-glucose** changed?

This question was not displayed to the respondent.

Q451. Why do you use compounded **deoxy-d-glucose** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q452. Do you stock non-patient-specific compounded **deoxy-d-glucose** in your practice location?

This question was not displayed to the respondent.

Q453. In what practice location(s) do you stock non-patient-specific compounded **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q454. How do you obtain your stock of non-patient-specific compounded **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q455. Why do you keep a stock of non-patient-specific compounded **deoxy-d-glucose**? Please check all that apply.

This question was not displayed to the respondent.

Q456. For which, if any, diseases or conditions do you consider **deoxy-d-glucose** standard therapy?

This question was not displayed to the respondent.

Q457. Does your specialty describe the use of **deoxy-d-glucose** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q458. What type(s) of product(s) do you use, prescribe, or recommend for **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q459. Please list any conditions or diseases for which you use compounded **diiodohydroxyquinoline** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q460.
Do you use compounded **diiodohydroxyquinoline** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q461. In which combination(s) do you use compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q462. For which, if any, diseases or conditions do you consider compounded **diiodohydroxyquinoline** standard therapy?

This question was not displayed to the respondent.

Q463. Does your specialty describe the use of compounded **diiodohydroxyquinoline** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q464. Over the past 5 years, has the frequency in which you have used compounded **diiodohydroxyquinoline** changed?

This question was not displayed to the respondent.

Q465. Why do you use compounded **diiodohydroxyquinoline** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q466. Do you stock non-patient-specific compounded **diiodohydroxyquinoline** in your practice location?

This question was not displayed to the respondent.

Q467. In what practice location(s) do you stock non-patient-specific compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q468. How do you obtain your stock of non-patient-specific compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q469. Why do you keep a stock of non-patient-specific compounded **diiodohydroxyquinoline**? Please check all that apply.

This question was not displayed to the respondent.

Q470. For which, if any, diseases or conditions do you consider **diiodohydroxyquinoline** standard therapy?

This question was not displayed to the respondent.

Q471. Does your specialty describe the use of **diiodohydroxyquinoline** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q472. What type(s) of product(s) do you use, prescribe, or recommend for **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q473. Please list any conditions or diseases for which you use compounded **diphenylcyclopropenone (DPCP)** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q474.
Do you use compounded **diphenylcyclopropenone (DPCP)** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q475. Please list all combination products in which you use compounded **diphenylcyclopropenone (DPCP)**.

This question was not displayed to the respondent.

Q476. For which, if any, diseases or conditions do you consider compounded **diphenylcyclopropenone (DPCP)** standard therapy?

This question was not displayed to the respondent.

Q477. Does your specialty describe the use of compounded **diphenylcyclopropenone (DPCP)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q478. Over the past 5 years, has the frequency in which you have used compounded **diphenylcyclopropenone (DPCP)** changed?

This question was not displayed to the respondent.

Q479. Why do you use compounded **diphenylcyclopropenone (DPCP)** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q480. Do you stock non-patient-specific compounded **diphenylcyclopropenone (DPCP)** in your practice location?

This question was not displayed to the respondent.

Q481. In what practice location(s) do you stock non-patient-specific compounded **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q482. How do you obtain your stock of non-patient-specific compounded **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q483. Why do you keep a stock of non-patient-specific compounded **diphenylcyclopropenone (DPCP)**? Please check all that apply.

This question was not displayed to the respondent.

Q484. For which, if any, diseases or conditions do you consider **diphenylcyclopropenone (DPCP)** standard therapy?

This question was not displayed to the respondent.

Q485. Does your specialty describe the use of **diphenylcyclopropenone (DPCP)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q486. What type(s) of product(s) do you use, prescribe, or recommend for **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q487. Please list any conditions or diseases for which you use compounded **podophyllum** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q488.
Do you use compounded **podophyllum** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q489. In which combination(s) do you use compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q490. For which, if any, diseases or conditions do you consider compounded **podophyllum** standard therapy?

This question was not displayed to the respondent.

Q491. Does your specialty describe the use of compounded **podophyllum** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q492. Over the past 5 years, has the frequency in which you have used compounded **podophyllum** changed?

This question was not displayed to the respondent.

Q493. Why do you use compounded **podophyllum** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q494. Do you stock non-patient-specific compounded **podophyllum** in your practice location?

This question was not displayed to the respondent.

Q495. In what practice location(s) do you stock non-patient-specific compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q496. How do you obtain your stock of non-patient-specific compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q497. Why do you keep a stock of non-patient-specific compounded **podophyllum**? Please check all that apply.

This question was not displayed to the respondent.

Q498. For which, if any, diseases or conditions do you consider **podophyllum** standard therapy?

This question was not displayed to the respondent.

Q499. Does your specialty describe the use of **podophyllum** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q500. What type(s) of product(s) do you use, prescribe, or recommend for **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q501. Please list any conditions or diseases for which you use compounded **podophyllum resin** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q502.
Do you use compounded **podophyllum resin** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q503. In which combination(s) do you use compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q504. For which, if any, diseases or conditions do you consider compounded **podophyllum resin** standard therapy?

This question was not displayed to the respondent.

Q505. Does your specialty describe the use of compounded **podophyllum resin** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q506. Over the past 5 years, has the frequency in which you have used compounded **podophyllum resin** changed?

This question was not displayed to the respondent.

Q507. Why do you use compounded **podophyllum resin** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q508. Do you stock non-patient-specific compounded **podophyllum resin** in your practice location?

This question was not displayed to the respondent.

Q509. In what practice location(s) do you stock non-patient-specific compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q510. How do you obtain your stock of non-patient-specific compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q511. Why do you keep a stock of non-patient-specific compounded **podophyllum resin**? Please check all that apply.

This question was not displayed to the respondent.

Q512. For which, if any, diseases or conditions do you consider **podophyllum resin** standard therapy?

This question was not displayed to the respondent.

Q513. Does your specialty describe the use of **podophyllum resin** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q529. What type(s) of product(s) do you use, prescribe, or recommend for **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q530. Please list any conditions or diseases for which you use compounded **quinacrine** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

This question was not displayed to the respondent.

Q531.
Do you use compounded **quinacrine** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

This question was not displayed to the respondent.

Q532. Please list all combination products in which you use compounded **quinacrine**.

This question was not displayed to the respondent.

Q533. For which, if any, diseases or conditions do you consider compounded **quinacrine** standard therapy?

This question was not displayed to the respondent.

Q534. Does your specialty describe the use of compounded **quinacrine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q535. Over the past 5 years, has the frequency in which you have used compounded **quinacrine** changed?

This question was not displayed to the respondent.

Q536. Why do you use compounded **quinacrine** instead of any FDA-approved drug product?

This question was not displayed to the respondent.

Q537. Do you stock non-patient-specific compounded **quinacrine** in your practice location?

This question was not displayed to the respondent.

Q538. In what practice location(s) do you stock non-patient-specific compounded **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q539. How do you obtain your stock of non-patient-specific compounded **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q540. Why do you keep a stock of non-patient-specific compounded **quinacrine**? Please check all that apply.

This question was not displayed to the respondent.

Q541. For which, if any, diseases or conditions do you consider **quinacrine** standard therapy?

This question was not displayed to the respondent.

Q542. Does your specialty describe the use of **quinacrine** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q543. What type(s) of product(s) do you use, prescribe, or recommend for **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

- [x] Compounded drug product
- [ ] FDA-approved drug product
- [ ] Over the counter drug product
- [ ] Dietary supplement (e.g. vitamin or herbal supplement products sold in retail setting)
- [ ] Unsure

Q544. Please list any conditions or diseases for which you use compounded **squaric acid dibutyl ester (SADBE)** in your practice. Please include the strength(s), dosing frequency(ies), dosage form(s), route(s) of administration, duration of therapy, and patient population (ex. age, gender, comorbidities, allergies, etc).

	Strength(s) (please include units)	Dosing frequency(ies)	Dosage form(s)	Route(s) of administration	Duration of therapy	Patient population
Condition 1 (please describe): Alopecia areata	1%	daily	solution	topical	as long as beneficial	adult/ male and female
Condition 2 (please describe)						

Condition 3 (please describe)

Condition 4 (please describe)

Condition 5 (please describe)

Condition 6 (please describe)

Condition 7 (please describe)

Condition 8 (please describe)

Q545.
Do you use compounded **squaric acid dibutyl ester (SADBE)** as a single agent active ingredient, or as one active ingredient in a combination product? Please check all that apply.

- [x] Single
- [ ] Combination

Q546. Please list all combination products in which you use compounded **squaric acid dibutyl ester (SADBE)**.

This question was not displayed to the respondent.

Q547. For which, if any, diseases or conditions do you consider compounded **squaric acid dibutyl ester (SADBE)** standard therapy?

Alopecia areata

Q548. Does your specialty describe the use of compounded **squaric acid dibutyl ester (SADBE)** in medical practice guidelines or other resources?

Yes

Q549. Over the past 5 years, has the frequency in which you have used compounded **squaric acid dibutyl ester (SADBE)** changed?

- (●) Yes - I use it **MORE** often now (briefly describe why) lack of other effective treatment for severe alopecia aerate
- ( ) Yes - I use it **LESS** often now (briefly describe why)
- ( ) No - use has remained consistent

Q550. Why do you use compounded **squaric acid dibutyl ester (SADBE)** instead of any FDA-approved drug product?

No approve FDA product available

Q551. Do you stock non-patient-specific compounded **squaric acid dibutyl ester (SADBE)** in your practice location?

- ( ) Yes
- (●) No

Q552. In what practice location(s) do you stock non-patient-specific compounded **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q553. How do you obtain your stock of non-patient-specific compounded **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q554. Why do you keep a stock of non-patient-specific compounded **squaric acid dibutyl ester (SADBE)**? Please check all that apply.

This question was not displayed to the respondent.

Q555. For which, if any, diseases or conditions do you consider **squaric acid dibutyl ester (SADBE)** standard therapy?

This question was not displayed to the respondent.

Q556. Does your specialty describe the use of **squaric acid dibutyl ester (SADBE)** in medical practice guidelines or other resources?

This question was not displayed to the respondent.

Q16. What is your terminal clinical degree? Please check all that apply.

- [x] Doctor of Medicine (MD)
- [ ] Doctor of Osteopathic Medicine (DO)
- [ ] Doctor of Medicine in Dentistry (DMD/DDS)
- [ ] Naturopathic Doctor (ND)
- [ ] Nurse Practitioner (NP)
- [ ] Physician Assistant (PA)
- [ ] Other (please describe)

Q17. Which of the following Board certification(s) do you hold? Please check all that apply.

- [ ] No Board certification
- [ ] Allergy and Immunology
- [ ] Anesthesiology
- [ ] Cardiovascular Disease
- [ ] Critical Care Medicine
- [x] Dermatology
- [ ] Emergency Medicine
- [ ] Endocrinology, Diabetes and Metabolism
- [ ] Family Medicine
- [ ] Gastroenterology
- [ ] Hematology
- [ ] Infectious Disease
- [ ] Internal Medicine
- [ ] Medical Toxicology
- [ ] Naturopathic Doctor
- [ ] Naturopathic Physician
- [ ] Nephrology
- [ ] Neurology
- [ ] Obstetrics and Gynecology
- [ ] Oncology
- [ ] Ophthalmology
- [ ] Otolaryngology
- [ ] Pain Medicine
- [ ] Pediatrics
- [ ] Psychiatry
- [ ] Rheumatology
- [ ] Sleep Medicine
- [ ] Surgery (please describe)
- [ ] Urology
- [ ] Other (please describe)