

# Summary Report

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## Podophyllum Resin

### Prepared for:

Food and Drug Administration

Clinical use of bulk drug substances nominated for inclusion on the 503B Bulks List

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### Prepared by:

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

University of Maryland School of Pharmacy

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## REVIEW OF NOMINATIONS

Podophyllum resin (UNII code: 16902YVY2B) was nominated for inclusion on the 503B Bulks List by the Outsourcing Facilities Association (OFA). While the exact medical condition for which the compounded product is being requested may be unknown, podophyllum resin is generally used to treat warts. The substance will be compounded into a topical liquid with strengths per the prescriber's request; the therapeutic dose is 5%. Podophyllum resin was nominated for use in combination with additional active pharmaceutical ingredients (API); see Table 7 for the nominated combination formulation.

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

- There are no FDA-approved drugs that contain this API.
- Compounding from bulk will ensure that no irritating, hazardous, or allergenic ingredients are included.
- Commercially available finished products have an inherent variance in potency creating an uncertain final concentration for the new product.

## METHODOLOGY

### *Background information*

The national medicine registers of 13 countries and regions were searched to establish the availability of podophyllum resin 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 podophyllum resin; name variations of podophyllum resin 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 routes of administration 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 podophyllum resin. The availability of OTC products (yes/no) in the US and the ROA of these products were recorded in a spreadsheet. Individual product information was not recorded.

## *Systematic literature review*

### Search strategy

A medical librarian constructed comprehensive search strategies for PubMed and Embase. The search strategies used a combination of controlled vocabulary terms and keywords to describe three (3) concepts: podophyllum resin; nominated indications and combinations; nominated ROA and dosage form (see Appendix 1 for full search strategies). Results were limited to original research articles or conference abstracts in English language. All searches were conducted on July 22, 2019.

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

### Study selection

Literature reviews and/or meta-analyses, cost-effectiveness, and epidemiological studies were excluded. Articles were considered relevant based on the identification of a clinical use of podophyllum resin or the implementation of podophyllum resin 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.

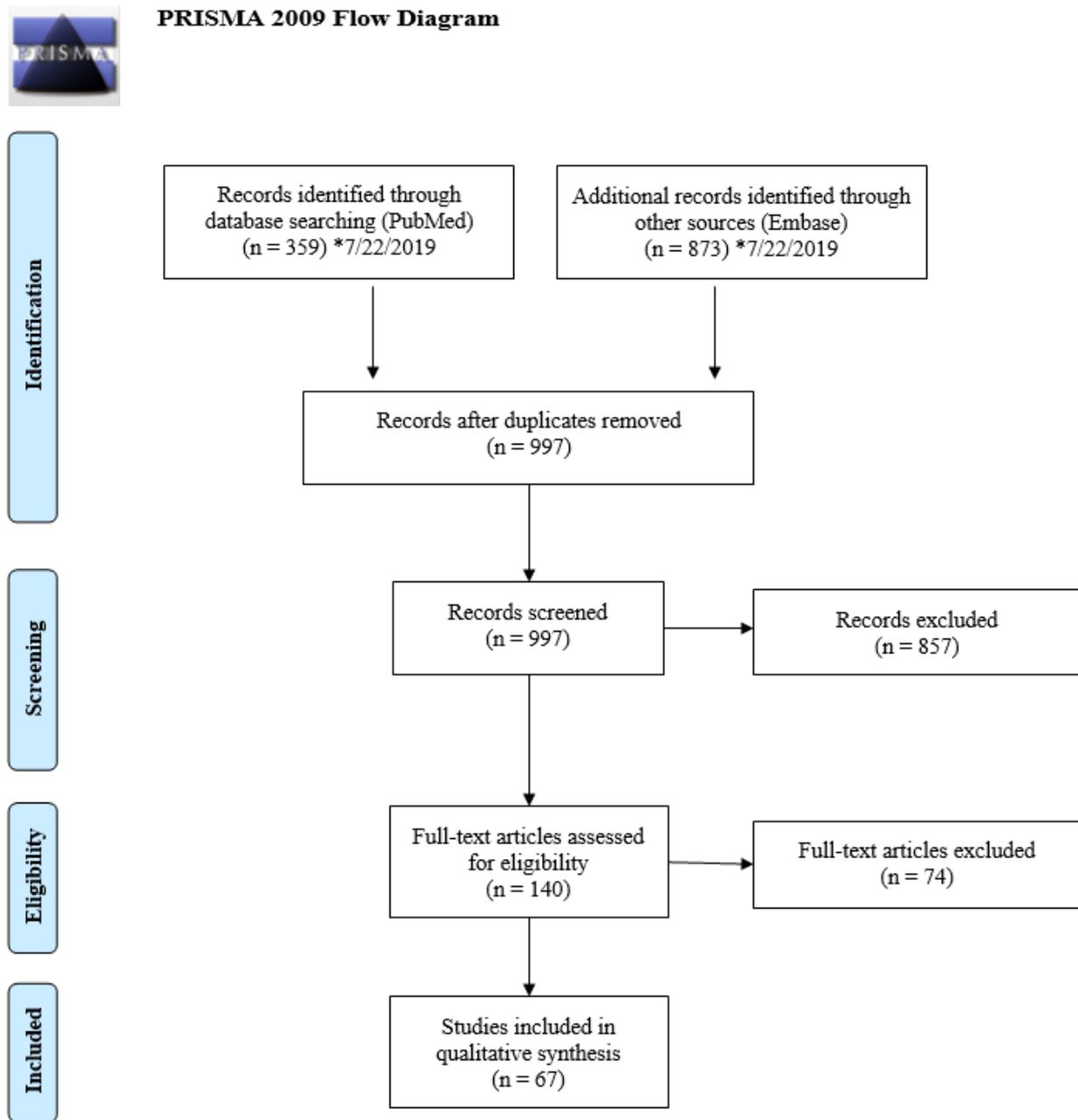
### Data extraction

A standard data extraction form was used to collect study authors; article title; year published; journal title; country; indication for podophyllum resin 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 podophyllum resin 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). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit [www.prisma-statement.org](http://www.prisma-statement.org).

### *Outreach to medical specialists and specialty organizations*

Using the indications from the nominations and the results of the literature review, three (3) medical specialties that would potentially use podophyllum resin were identified: dermatology, obstetrics and gynecology, 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. One (1) expert was contacted for interviews, of which one (1) accepted and zero (0) declined interviews. One (1) medical expert with a Doctor of Medicine (MD) specializing in oncology was contacted, however the interviewee failed to respond to the interview request. All 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 RIIHSC 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, obstetrics and gynecology, and oncology, identified from the nominations and literature review, 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 six (6) 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

<b>Specialty</b>	<b>Association</b>
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
Obstetrics and Gynecology	American College of Obstetricians and Gynecologists (ACOG)	Declined, survey not approved for distribution
Oncology	American Society of Clinical Oncology (ASCO)	Declined

## CURRENT AND HISTORIC USE

### *Summary of background information*

- Podophyllum resin is not available as an FDA-approved product.
- Podophyllum resin is not available as an OTC product in the US.
- There is a current United States Pharmacopeia (USP) monograph for podophyllum resin.
- Podophyllum resin is available in Canada as a single-agent product and as a combination product in Australia, Latvia, and Hong Kong.

Table 3. Currently approved products – US

*No approved products in the US*

Table 4. Currently approved products—select non-US countries and regions<sup>a</sup>

Active Ingredient	Concentration	Dosage Form	ROA	Approved For Use		
				Country	Status	Approval Date <sup>b</sup>
Podophyllin	250mg/mL	Liquid	Topical	Canada	Prescription	12/31/1984

Abbreviations: ROA, route of administration.

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

<sup>b</sup>If multiple approval dates and/or multiple strengths, then earliest date provided.

### Summary of literature review

- Total number of studies included: 67 studies (30 descriptive, 34 experimental, and 3 observational).
- Most of the studies were from the US (21 studies).
- The most common indication for the use of podophyllum resin in the US and non-US studies was genital warts.
- Compounded products were identified from both US and non-US studies. One of the US studies utilized podophyllum resin as the nominated compounded formulation.

Table 5. Types of studies

Types of Studies	Number of Studies
Descriptive <sup>1-30</sup>	30
Experimental <sup>31-64</sup>	34
Observational <sup>65-67</sup>	3

Table 6. Number of studies by country

Country	Number of Studies
Brazil <sup>50,51</sup>	2
Cuba <sup>35</sup>	1
Denmark <sup>20,30,41</sup>	3
Egypt <sup>37</sup>	1
Finland <sup>45</sup>	1
India <sup>4,5,24,27,43,48,52,56,61</sup>	9
Iran <sup>1,31,60</sup>	3
Iraq <sup>67</sup>	1
Italy <sup>21</sup>	1
Nigeria <sup>9,28,53,54</sup>	4
Poland <sup>49</sup>	1
Singapore <sup>38,46</sup>	2

South Korea <sup>14,15</sup>	2
Sweden <sup>40,62</sup>	2
UK <sup>6,26,32-34,36,42,44,57,58,63</sup>	12
US <sup>2,3,7,10-13,16-19,22,23,25,29,39,47,55,59,65,66</sup>	21
Multiple Countries <ul style="list-style-type: none"> <li>• UK, Finland, Italy, Belgium Denmark<sup>64</sup></li> </ul>	1
Total US: 21 Total Non-US Countries: 46	

Table 7. Number of studies by combinations

	Combination Formula	Number of Studies
<b>Nominated</b>	Podophyllum resin 5% / Cantharidin 1% / Salicylic acid 30% – Topical liquid <sup>26,65</sup>	2
<b>Others found in literature</b>	Podophyllum resin 20% / Cantharidin 1% / Salicylic acid 30% - Topical <sup>37</sup>	1
	Podophyllum resin 25% / Colchicine alkaloid 0.1% / F.E. Euphorbia 10% / Salicylic acid 10% - Topical <sup>11</sup>	1
	Podophyllum resin 25% / Salicylic acid 20% - Topical solution <sup>13</sup>	1
	Podophyllum resin 25% / TCA 50% - Topical solution <sup>36</sup>	1

Table 8. Dosage by indication – US

Indication	Dose	Concentration	Dosage Form	ROA	Duration of Treatment
Genital warts <sup>2,3,7,10,12,18,19,22,29,55,59,66</sup>	–	10-25%	Solution	Topical	1-2 sessions
	–	20-25%	Tincture		6-9 sessions
	–	25%	Suspension		1-4 sessions
	–	25%	Suspension	–	–
	–	25%	–	–	5 weeks
Hairy leukoplakia <sup>17,25,39,47</sup>	–	25%	Solution	Topical	Once
	–	25%	–	–	–
Plantar warts <sup>11,16,65</sup>	–	25%	Suspension	Topical	3-4 sessions
	–	5-25%	–		1-3 sessions

Cutaneous vegetations <sup>23</sup>	–	25%	Ointment	–	–
Senile keratosis <sup>13</sup>	–	25%	Solution	Topical	Once
Squamous micropapilloma <sup>55</sup>	–	25%	–	–	5 weeks

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

Table 9. Dosage by indication – non-US countries

Indication	Dose	Concentration	Dosage Form	ROA	Duration of Treatment
Genital warts <sup>4,6,9,14,21,24,27,28,31-33,35,36,38,40-46,48,49,52-54,56-58,60-64,67</sup>	0.5ml	0.25-25%	Solution	Topical	<ul style="list-style-type: none"> <li>• 3-4 sessions</li> <li>• 4-16 weeks</li> </ul>
	–	10-25%	Tincture		6-12 weeks
	–	20-25%	–		<ul style="list-style-type: none"> <li>• 1-11 sessions</li> <li>• 3-6 weeks</li> </ul>
	–	20%	Solution	–	At most 6 weeks
	–	25%	Tincture		6 weeks
	5ml	0.5-25%	–		6 weeks
Plantar warts <sup>8,34,37</sup>	–	25%	Suspension	Topical	–
	–	20-50%	–		1-5 sessions
Recalcitrant cutaneous wart <sup>26</sup>	–	5%	–	–	–
Buschke-Lowenstern tumor <sup>1,5,15</sup>	–	5-25%	Solution	Topical	6 sessions
	–	–	–		10 days

Basal cell carcinoma <sup>20,30</sup>	–	25%	Solution	–	–
	–	20%	–	–	–
Hairy leukoplakia <sup>50,51</sup>	–	25%	Solution	Topical	At most 25 weeks

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

Table 10. Compounded products – US

Indication	Publication Year	Compounding Method	Dosage Form	Final Strength
Genital warts <sup>2,7,29,59</sup>	1944-1990	<ul style="list-style-type: none"> <li>• "Prepared by pharmacist"</li> </ul>	Solution	10%
		<ul style="list-style-type: none"> <li>• In mineral oil</li> <li>• "Prepare a 25% suspension of podophyllin in mineral oil"</li> </ul>	Suspension	25%
		<ul style="list-style-type: none"> <li>• "25% podophyllin in tincture of benzoin compound was supplied by a local pharmacy"</li> </ul>	Tincture	25%
Hairy leukoplakia <sup>25,39,47</sup>	1992-1995	<ul style="list-style-type: none"> <li>• 25% solution of podophyllin in compound tincture of benzoin</li> <li>• In benzoin tincture</li> <li>• "Podophyllum resin 25% sol in benzoin compound tincture was prepared by our hospital pharmacy"</li> </ul>	Solution	25%
Plantar warts <sup>11,65</sup>	1980-1984	<ul style="list-style-type: none"> <li>• F.E. Euphorbia 10%, podophyllum resin 25%, salicylic acid 10%, colchicine alkaloid 0.1%, glacial acetic acid qs 100%</li> <li>• Salicylic acid 30%, podophyllin 5%, cantharidin 1%, penederm 0.5%</li> </ul>	–	5-25%
Cutaneous vegetations <sup>23</sup>	1947	<ul style="list-style-type: none"> <li>• 25% mixture of podophyllin (resin podophyllum, N.F.) in a water soluble base (hydrosorb)</li> </ul>	Ointment	25%
Senile keratosis <sup>13</sup>	1950	<ul style="list-style-type: none"> <li>• 25% podophyllin, 20% salicylic acid, in equal parts 95% alcohol and acetone</li> </ul>	Solution	25%

Abbreviation: “–”, not mentioned.

Table 11. Compounded products – non-US countries

Indication	Compounding Method	Dosage Form	Final Strength
Genital warts <sup>6,32,36,38,46,58,63</sup>	<ul style="list-style-type: none"> <li>• 7.5g podophyllin resin and 30ml methylated spirit</li> <li>• In methylated spirits</li> <li>• In benzoin tincture; podophyllin resin with ethanol</li> </ul>	Solution	0.25-25%
	<ul style="list-style-type: none"> <li>• 10% and 25% podophyllum emodi in tincture of benzoin compound (TBC) prepared in one pharmacy and dispensed in stock bottles</li> </ul>	Tincture	10-25%
	<ul style="list-style-type: none"> <li>• 25% podophyllin resin, 25% liquid paraffin, 25% soft paraffin</li> <li>• "Freshly prepared 25% podophyllin in tincture of benzoin compound"</li> <li>• Prepared in the Birmingham general hospital pharmacy from podophyllum hexandrum (emodii) derived podophyllin resin powder in 90% industrial methylated spirits</li> </ul>	–	0.5-25%
Buschke-Lowenstein tumor <sup>5</sup>	<ul style="list-style-type: none"> <li>• In benzoin tincture</li> </ul>	Solution	25%

Abbreviation: “–”, not mentioned.

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

One (1) interview was conducted.

Table 12. Overview of interviewee

Interviewee	Level of Training	Specialty	Current Practice Setting	Experience with podophyllum resin	Interview Summary Response
DER_06	MD	Dermatology/ Immunology	Independent consultant	Used in training	<ul style="list-style-type: none"> <li>• Hesitant in advocating the use of nominated combination (salicylic acid can change pH and affect the structure). Would use one ingredient at a time to see therapeutic response.</li> <li>• Prefers the pure form (podophyllum, podophylloxin, podofilox) over the extract form (podophyllum resin, podophyllin) due to low quality control and high variability in active pharmaceutical ingredient in the extract, which could be a risk to patient safety.</li> <li>• “I think there's still a law potentially for being able to treat somebody in the office. I'm not going to say we shouldn't have that be an option, that's the place where the bulk compounding comes into place.”</li> <li>• “If you're going to say that you're going to make one available. My preference in the office is to have the one in which you have better control over the API.”</li> </ul>

Abbreviation: MD, Doctor of Medicine.

*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

<b>Types of Products</b>	<b>Respondents, n (N=2<sup>a</sup>)</b>
Compounded	0
FDA-approved	1
Over-the-counter	0
Dietary	0
Unsure	0
No response	1

<sup>a</sup>Out of 5 respondents, 2 reported using, prescribing, or recommending podophyllum resin products.

Table 15. Compounded use of podophyllum resin in practice

*No survey respondents provided this information*

Table 16. Indications for which podophyllum resin is considered a standard therapy

<b>Indication</b>	<b>Standard therapy</b>		
	<b>Compounded, n (N=0)</b>	<b>Non-compounded, n (N=1)</b>	<b>No response, n (N=1)</b>
Condyloma acuminata	0	1	0
No response	0	0	1

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 podophyllum resin usage over the past 5 years

*No survey respondents provided this information*

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

*No survey respondents provided this information*

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

*No survey respondents provided this information*

## CONCLUSION

Podophyllum resin (UNII code: 16902YVY2B) was nominated for inclusion on the 503B Bulks List by the Outsourcing Facilities Association (OFA). While the exact medical condition for which the compounded product is being requested may be unknown, podophyllum resin is generally used to treat warts. The substance will be compounded into a topical liquid with strengths per the prescriber's request; the therapeutic dose is 5%. Podophyllum resin was nominated for use in combination with additional active pharmaceutical ingredients (API). Podophyllum resin is available in Canada as a single-agent product and as a combination product in Australia, Latvia, and Hong Kong.

From the literature review conducted, the most common indication in the US and non-US studies is genital warts. Compounded products were identified from both US and non-US studies.

From the interviews, the interviewee stated that there may be a potential for office use but would prefer the pure form (podophyllum) over the extract form (podophyllum resin). Interviewee was hesitant about the nominated combination.

From the survey responses, two (2) out of five (5) respondents used podophyllum resin, but none used a compounded product.

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## APPENDICES

### Appendix 1. Search strategies for bibliographic databases

#### MEDLINE search strategy

- Platform: PubMed
- Years searched: 1946 to present
- Limits: English language
- Date searched: July 22, 2019
- Number of results: 359

1	Search "podophyllin"[MeSH] OR podophyllin*[tiab] OR podofillin*[tiab] OR "podophyllum resin"[tiab] OR podophyllotoxin*[tiab] OR podofilotoxin*[tiab] OR podofyllotoxin*[tiab] OR podofilox[tiab] OR pododem[tiab] OR podoben[tiab] OR podofilia [tiab] OR podocon[tiab] OR podofilm [tiab] OR canthacur[tiab] OR condil[tiab] OR condiver[tiab] OR condyline[tiab] OR condylox[tiab] OR warix[tiab] OR wartec[tiab] OR warticon[tiab]))	2262
2	Search "warts"[MeSH] OR "keratosis"[MeSH] OR "leukoplakia"[MeSH] OR wart[tiab] OR warts[tiab] OR "condylomata acuminata"[tiab] OR verruca[tiab] OR verrucas[tiab] OR keratosis[tiab] OR keratosis[tiab] OR keratoma[tiab] OR keratomas[tiab] OR kera toderma[tiab] OR kera todermas[tiab] OR leukoplaki*[tiab] OR leukokeratosis[tiab] OR leukokeratosis[tiab] OR epithelioma*[tiab] OR "cantharidin"[MeSH] OR "salicylic acid"[MeSH] OR cantharidin*[tiab] OR "salicylic acid"[tiab]	69230
3	Search "administration, topical"[MeSH] OR "skin cream"[MeSH] OR "drug combinations"[MeSH] OR "drug compounding"[MeSH] OR "therapeutic use"[subheading] OR "drug therapy"[subheading] OR "administration and dosage"[subheading] OR topical[tiab] OR cream[tiab] OR liquid[tiab] OR solution[tiab] OR gel[tiab] OR treat*[tiab] OR therap*[tiab] OR compound*[tiab]	10089063
4	Search ("animals"[MeSH] NOT "humans"[MeSH])	4601331
5	Search (#1 AND #2 AND #3)	454
6	Search (#5 NOT #4)	447
7	Search (#6 AND English[lang])	359

#### Embase search strategy

- Platform: Elsevier
- Years searched: 1947 to present
- Limits: English language
- Date searched: July 22, 2019
- Number of results: 873

1	podophyllotoxin/de	3041
2	podophyllin/de	2212

3	podophyllin\$:ti,ab,tn	856
4	podofillin\$:ti,ab,tn	8
5	podophyllum resin\$:ti,ab,tn	37
6	podophyllotoxin\$:ti,ab,tn	1766
7	podofilotoxin\$:ti,ab,tn	0
8	podofyllotoxin\$:ti,ab,tn	2
9	podofilox':ti,ab,tn	65
10	pododerm':ti,ab,tn	1
11	podoben':ti,ab,tn	6
12	podofilia':ti,ab,tn	0
13	podocon':ti,ab,tn	6
14	podofilm':ti,ab,tn	0
15	canthacur':ti,ab,tn	7
16	condil':ti,ab,tn	2
17	condiver':ti,ab,tn	0
18	condyline':ti,ab,tn	60
19	condylox':ti,ab,tn	87
20	warix':ti,ab,tn	1
21	wartec':ti,ab,tn	42
22	warticon':ti,ab,tn	14
23	cantharone plus':ti,ab,tn	4
24	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23	5568
25	verruca vulgaris'/exp	10000
26	condyloma acuminatum'/exp	8587
27	keratosis'/exp	33304
28	keratoderma'/exp	5147

29	leukoplakia'/de	8157
30	epithelium tumor'/de	9432
31	wart\$:ti,ab	12183
32	condylomata accuminata'ti,ab	61
33	verruca\$:ti,ab	2063
34	keratosis':ti,ab	8002
35	keratoses':ti,ab	4058
36	keratoma'ti,ab	246
37	keratomas':ti,ab	45
38	keratoderma\$:ti,ab	2400
39	leukoplaki\$:ti,ab	5071
40	leukokeratosis':ti,ab	163
41	leukokeratoses':ti,ab	15
42	epithelioma\$:ti,ab	7968
43	cantharidin'/de	1501
44	salicylic acid'/de	25253
45	cantharidin\$:ti,ab,tn	1031
46	salicylic acid':ti,ab,tn	14047
47	#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46	108337
48	topical drug administration'/de OR 'cutaneous drug administration'/de OR 'topical agent'/de	81613
49	drug efficacy'/de	825116
50	drug formulation'/de	115479
51	drug therapy':lnk	3734469
52	drug combination':lnk	804980
53	drug comparison':lnk	582238
54	topical\$:ti,ab	129240

55	#48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54	4497527
56	#24 AND #47 AND #55	1337
57	[animals]/lim NOT [humans]/lim	5871425
58	#56 NOT #57	1323
59	#56 NOT #57 AND [english]/lim	969
60	#56 NOT #57 AND [english]/lim AND ([article]/lim OR [article in press]/lim OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [data papers]/lim OR [review]/lim OR [short survey]/lim)	873

## Appendix 2. 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 **podophyllum resin**. 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](mailto: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](mailto:hrpo@umaryland.edu).

### End of Block: Welcome Page

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### Start of Block: Podophyllum resin

Q1. What type(s) of product(s) do you use, prescribe, or recommend for **podophyllum resin**? 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 podophyllum resin? Please check all th... != Compounded drug product*

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

---

### Display This Question:

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

Q2. 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).

	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 **podophyllum resin** 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 podophyllum resin as a single agent active ingredient, or as one active ingredient... != Combination*

*Display This Question:*

*If Loop current: Do you use compounded podophyllum resin as a single agent active ingredient, or as one active ingredient... = Combination*

Q4. In which combination(s) do you use compounded **podophyllum resin**? Please check all that apply.

- Podophyllum resin 5% / Cantharidin 1% / Salicylic acid 30%
- Other (please describe) \_\_\_\_\_

Q5. For which, if any, diseases or conditions do you consider compounded **podophyllum resin** standard therapy?

\_\_\_\_\_

Q6. Does your specialty describe the use of compounded **podophyllum resin** in medical practice guidelines or other resources?

\_\_\_\_\_

Q7. Over the past 5 years, has the frequency in which you have used compounded **podophyllum resin** 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

Q8. Why do you use compounded **podophyllum resin** instead of any FDA-approved drug product?

\_\_\_\_\_

Q9. Do you stock non-patient-specific compounded **podophyllum resin** in your practice location?

- Yes
- No

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

*Display This Question:*

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

Q10. In what practice location(s) do you stock non-patient-specific compounded **podophyllum resin**? Please check all that apply.

- Physician office
- Outpatient clinic
- Emergency room
- Operating room
- Inpatient ward
- Other (please describe) \_\_\_\_\_

Q11. How do you obtain your stock of non-patient-specific compounded **podophyllum resin**? Please check all that apply.

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

Q12. Why do you keep a stock of non-patient-specific compounded **podophyllum resin**? 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 podophyllum resin? Please check all that apply. = Convenience*

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

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

Q13. For which, if any, diseases or conditions do you consider **podophyllum resin** standard therapy?

\_\_\_\_\_

Q14. Does your specialty describe the use of **podophyllum resin** in medical practice guidelines or other resources?

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End of Block: Podophyllum resin

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Start of Block: Background Information

Q15. 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) \_\_\_\_\_

Q16. 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**