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### **Supplemental Material**

#### **A Systematic Review of Mercury Exposures from Skin-Lightening Products**

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**Figure S1.** PRISMA flow diagram detailing how articles were identified, reviewed, and deemed eligible for inclusion in the current study.

#### **References**

**Additional File-** Excel Document

**Table S1.** Measurement instruments and abbreviations used for skin-lightening product analysis. These data cover 738 product samples from 25 studies.

<b>Measurement instrument used for testing skin-lightening products</b>	<b>No. of samples (%)</b>
Atomic absorption spectroscopy (AAS)	94 (11.94%)
Screen-printed silver electrode (AgSPE)	3 (0.38%)
Cold vapor atomic absorption spectrometry (CVAAS)	466 (59.21%)
Flame atomic absorption spectrometry (FAAS)	6 (0.76%)
Inductively coupled plasma mass spectrometry (ICP-MS)	38 (4.83%)
Inductively coupled plasma-optical emission spectrometry (ICP-OES)	78 (9.91%)
Inductively coupled plasma atomic emission spectrometry (ICP-AES)	49 (6.23%)
Particle Induced X-Ray Emission (PIXE)	27 (3.43%)
Unknown	26 (3.30%)

**Table S2.** Measurement instruments and abbreviations used for human biomarker analysis. These data cover 1,042 biomarker measures from 9 studies.

<b>Measurement instrument used for testing human biomarkers</b>	<b>No. of samples (%)</b>
Atomic absorption spectroscopy (AAS)	40 (3.8%)
Advanced mercury analyzer (AMA)	62 (6.0%)
Cold vapor atomic absorption spectrometry (CVAAS)	11 (1.1%)
Inductively coupled plasma mass spectrometry (ICP-MS)	13 (1.3%)
Particle Induced X-Ray Emission (PIXE)	148 (3.4%)
Unknown	768 (73.7%)

**Table S3.** Different toxic chemicals measured in papers in the “Hg in products” data group.

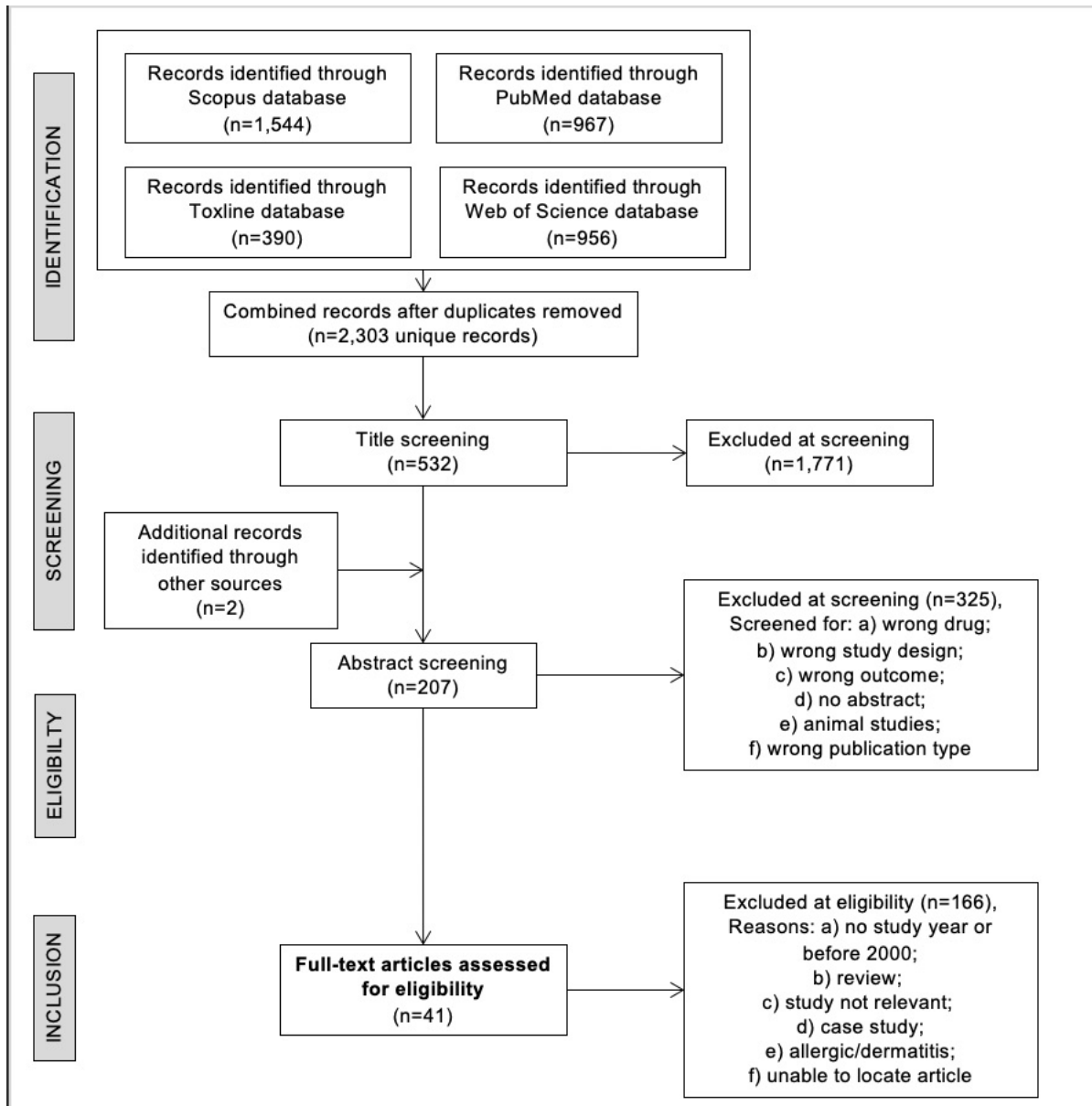
No.	Author, year	Chemicals measured
1	Agorku et al., 2016 <sup>1</sup>	Mercury, Hydroquinone
2	Murphy et al., 2009 <sup>2</sup>	Mercury
3	Ho et al., 2017 <sup>3</sup>	Mercury
4	Zainy, 2015 <sup>4</sup>	Mercury, Cadmium, Bismuth, Palladium, Arsenic, Titanium, Titanium dioxide, Thallium
5	Harada et al., 2001 <sup>5</sup>	Mercury
6	Peregrino et al., 2011 <sup>6</sup>	Mercury
7	Gbetoh & Amyot, 2016 <sup>7</sup>	Mercury, hydroquinone and clobetasol propionate
8	Al-Saleh et al., 2012 <sup>8</sup>	Mercury, Titanium dioxide, Hydroquinone, Corticosteroids,
9	Yang et al., 2014 <sup>9</sup>	Mercury
10	Salama, 2016 <sup>10</sup>	Lead, Mercury, Cadmium, Arsenic, Copper, Nickel, Cobalt, Manganese, Chromium, Aluminum
11	Wang & Zhang, 2015 <sup>11</sup>	Mercury
12	McKelvey et al., 2011 <sup>12</sup>	Mercury
13	Ashraf et al., 2020 <sup>13</sup>	Mercury, Cadmium, Lead, Arsenic, Chromium, Nickel, Cobalt, Copper, Zinc, Iron
14	Selvaraju et al., 2020 <sup>14</sup>	Mercury, Arsenic, Cadmium, Lead
15	Abbas et al., 2020 <sup>15</sup>	Mercury
16	Kanwal et al., 2019 <sup>16</sup>	Mercury
17	Kinabo, 2005 <sup>17</sup>	Mercury
18	Voegborlo et al., 2008 <sup>18</sup>	Mercury
19	Alqadami et al., 2017 <sup>19</sup>	Mercury, Arsenic, Bismuth, Cadmium, Lead, Titanium
20	Alqadami et al., 2013 <sup>20</sup>	Mercury, Arsenic, Bismuth, Cadmium, Lead, Titanium
21	Maneli et al., 2016 <sup>21</sup>	Mercury, Betamethasone, Clobetasol propionate, Hydroquinone; Kojic acid
22	Ababneh & Al-Momani, 2018 <sup>22</sup>	Mercury, Lead, Cadmium, Nickel
23	Mohammed et al., 2017 <sup>23</sup>	Mercury, Arsenic
24	Amponsah et al., 2014 <sup>24</sup>	Mercury
25	Cristaudo et al., 2013 <sup>25</sup>	Mercury, Cadmium, Cobalt, Chromium, Nickel, Lead

**Table S4.** Case reports of individuals that experienced an adverse reaction following exposure to a mercury-added skin-lightening product. AFRO = African Region; EMRO = Eastern Mediterranean Region; EURO = European Region; PAHO = Pan America Health Region; SEARO = South-East Asia Region; WPRO = Western Pacific Region.

Authors, year	Ethnicity/ Race	Country	WHO Region	Clinical Details
Drescher et al., 2013 <sup>26</sup>	Barbadian	Barbados	PAHO	In 2010, high mercury exposure was discovered in four Barbadian women of African ancestry (aged 39-54) during a study analyzing mercury body-burden amongst individuals working in the fishing industry. All women were using or previously used skin-lightening creams, and had hair inorganic mercury concentrations 361-561 µg/g and spot urine inorganic mercury samples 7-135 µg/L.
Soo et al., 2003 <sup>27</sup>	Indonesian	China	WPRO	A 34-year-old Indonesian woman working in Hong Kong for a year and had two weeks of frothy urine and ankle swelling after applying an Indonesian skin-lightening cream on her face every day for five years. She had elevated blood mercury levels of 163nmol/L (59.09 µg/L) and a 24-hour urinary mercury excretion rate of 754.6nmol/day, and the mercury concentration of the cream was 1762 µg/g.
Sun et al., 2017 <sup>28</sup>	Chinese	China	WPRO	From 2009 to 2017, 16 patients (aged 19-50 years) that had a history of using skin lightening creams (one product contained 19,742 ± 379 µg/g of mercury) were diagnosed with chronic mercury intoxication. All patients had a 24-hour urine mercury content of these patients was within 0.037-0.170 mg/L (37 µg/L to 170 µg/L), and patients mentioned body pain, tremors, insomnia, irritability and depression.
Dickenson et al., 2013 <sup>29</sup>	Mexican	USA	PAHO	A research study assessing environmental chemical exposure in pregnant women and their infants identified 1 participant out of 77 that had elevated levels of mercury (whole blood mercury level 15.16 µg/L, umbilical cord blood: 5.8 µg/L and urine mercury level 40 µg/L). The participant had been using two skin-lightening creams purchased in Mexico containing 21,000 and 30,000 µg/g of mercury.
Bwomda et al., 2005 <sup>30</sup>	African	Belgium	EURO	A 24-year-old African woman presented at the emergency department six months after developing symptoms including glucocorticosteroid induced arterial hypertension, weight gain, amenorrhea, and signs of Cushing's syndrome after full body application of a skin-lightening cream for ~10 years.
Chakera et al., 2011 <sup>31</sup>	Pakistani	United Kingdom	EURO	Two Pakistani women (aged 44 and 26 years) were referred for investigation of the nephrotic syndrome after renal biopsies showed that they had membranous glomerulonephritis associated to usage of skin-lightening creams. Their serum and urinary mercury-creatinine ratio was 150nmol/L and 16.5nmol/mmol, and 233 nmol/l and 77.5nmol/mmol, respectively.

Ori et al., 2018 <sup>32</sup>	Not indicated	USA	PAHO	A 17-month-old toddler experienced three weeks symptoms including fussiness, constipation, and decreased appetite after being in contact with their mother and grandmother who were using skin-lightening creams. Toddler's whole blood mercury was 26 µg/L, and random spot mercury level of 243 µg/g creatinine. Mother and grandmother had elevated first void urine mercury levels of 197 µg/g creatinine and 222 µg/g creatinine, respectively, and skin-lightening cream contained mercury levels between 27,000 and 34,000 µg/g.
Copan et al., 2015 <sup>33</sup>	Not indicated	USA	PAHO	From 2010-2014, two infants and an adult, 20-month-old, 4-year-old, and 39-year-old, respectively, had elevated mercury levels between 52 µg/g to 482 µg/g creatinine, all associated with skin-lightening creams containing mercury levels between 20,000-57,000 µg/g.
Zhang et al., 2014 <sup>34</sup>	Chinese	China	WPRO	In 2010, a woman (aged 28-year-old) was admitted to the hospital after complaining for two weeks of pain in both limbs and facial edema and was diagnosed with nephrotic syndrome. She used a homemade skin-lightening cream for 11 months that contained 6.80 µg/g, and her blood and urinary mercury concentration was 220 µmol/L and 469 µmol/L, respectively.
Tlacuilo-Parra et al., 2001 <sup>35</sup>	Mexican?	Mexico	PAHO	In 1996, a woman (aged 30-year-old) experienced burning face pain and excessive perspiration after using a daily facial skin-lightening cleanser listed with calomel for five years. Her urine mercury was 150 µg/L and whole blood mercury was µg/L.
Tang et al., 2006 <sup>36</sup>	Chinese	Hong Kong	WPRO	A Chinese woman (aged 34-year-old) developed nephrotic syndrome, minimal change disease and increased mercury concentrations in blood (24.8 µg/L) and urine (57.4 µg/L) after daily usage of a skin-lightening cream contain 30,000 µg/g of mercury for 4 months. Her proteinuria returned to normal after 9 months, and her blood and urine became normal after 1 and 9 months respectively after cessation of usage.
Rakete et al., 2021 <sup>37</sup>	Not indicated	Not indicated	EURO	A child (aged 4-year-old) was admitted to the hospital with symptoms including hypertension, increased sweating, behavioral changes and weight loss, and examinations revealed acute mercury poisoning. The child's mercury levels were 19 µg/L in urine and 37 µg/L in blood. The child's mother was using a facial cream bought online, containing approximately 18% mercury and the child was accidentally intoxicated by skin-to-skin contact with the mother.
Chan et al., 2001 <sup>38</sup>	Chinese	Hong Kong	WPRO	A woman (aged 38-year-old) had an asymptomatic increase in blood mercury concentration (18.8 µg/L) and a urine mercury excretion (69 µg/day) after daily use of a cosmetic cream for several months. The cream contained 6.5% mercury.
Barit et al., 2020 <sup>39</sup>	Filipino	Philippines	WPRO	A Filipino woman (aged 27-year-old) presented pruritic erythematous papules and plaques on the bilateral axillae after using a skin-lightening cream containing 6400 µg/g of mercury.

Kuehn, 2020 <sup>40</sup>	Mexican American	USA	PAHO	A Mexican American woman (aged 47-year-old) developed dysesthesias and upper extremity weakness and hospitalized for two weeks with slurred speech and blurry vision after using two skin-lightening creams on her face twice daily for 7 years. She had blood mercury levels of 2620 µg/L and urinary mercury levels of 110 µg/L and underwent chelation therapy. Skin-lightening creams were purchased in Mexico and contained 12,000 µg/g of mercury; further testing of creams detected methyl mercury iodide.
Kamani et al., 2019 <sup>41</sup>	Not indicated	USA	PAHO	An infant (aged ten-month-old) was admitted to hospital with a one-month of symptoms including of a progressive desquamative papular rash, anorexia, weight loss and hypertension. Patient had whole blood mercury levels at 251 nmol/L and underwent empiric succimer chelation therapy for three weeks. The patient's mother purchased a locally made skin cream in Mexico containing elemental mercury at 56,000 µg/g and had been using it on her face/neck twice daily for 6 weeks before onset of patient's symptoms.



**Figure S1.** PRISMA flow diagram detailing how articles were identified, reviewed, and deemed eligible for inclusion in the current study.



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