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13 **SUPERIOR COURT OF THE STATE OF CALIFORNIA**

14 **FOR THE COUNTY OF LOS ANGELES**

15 JENNIFER ROBI,

16 Plaintiff,

17 v.

18 MERCK & CO., INC., a New Jersey Corporation,
19 MERCK SHARP & DOHME CORP., a New Jersey
20 Corporation, KAISER FOUNDATION
21 HOSPITALS, a Corporation; SOUTHERN
22 CALIFORNIA PERMANENTE MEDICAL
23 GROUP; JUDITH GARZA, MD., CLAIRE
24 VALENCIA FULLER, M.D., ROBIN B.
25 SCANLON, M.D.; AND DOES 1 through 100,

26 Defendants.

Case No. BC628589

Hon. Elaine Lu

**AMENDED DECLARATION
OF STEPHEN AMATO, PhD,
MBA**

Dept.: SS-9
Action Filed: July 27, 2016
Trial Date: January 21, 2025

*[Filed concurrently with Amended Declaration
of Bijan Esfandiari in Support of Amended
Declaration of Stephen Amato, Ph.D., MBA]*

1 **DECLARATION OF STEPHEN AMATO**

2 I, Stephen Amato, declare and state as follows:

- 3 1. Attached hereto as **Exhibit 1** is a true and correct copy of the Expert Report I prepared in this
4 case. Appended to my Report is a true and correct copy of my curriculum vitae. This Declaration
5 does not set forth in detail everything that is included in my Report. Rather, I have attempted to
6 distill the highlights of my Report to points that I believe will be helpful to the Court. However,
7 this Declaration is not intended to be a substitute for my Report, which sets forth my opinions
8 and grounds for my opinions in greater detail.
- 9 2. The statements and opinions contained in my Report are true and correct to the best of my
10 knowledge, information, and belief, and I incorporate them by reference herein.
- 11 3. The statements and opinions contained in this Declaration are offered within a reasonable
12 degree of scientific and regulatory certainty and are true and correct to the best of my
13 knowledge, information, and belief.

14 **SUMMARY OF QUALIFICATIONS**

- 15
- 16
- 17 4. I am a global regulatory affairs professional with 25 years of direct biomedical product and
18 associated services commercialization experience. I have consistently demonstrated expert-
19 level proficiency in driving business growth in diverse global markets by solving complex
20 regulatory affairs and marketing associated challenges in the pharmaceutical, medical device,
21 combination product, companion diagnostics, and in vitro diagnostics sectors.
- 22 5. I have obtained a bachelor's degree in biochemical sciences from Harvard University, a Ph.D.
23 in molecular and cellular biology from Boston College, and a MBA from Boston College's
24 Carroll School of Management.
- 25 6. I currently serve as Full Professor and Department Chair for Global Regulatory Affairs, Quality
26 Assurance & Advanced Manufacturing at the College of Professional Studies (CPS) at
27 Northeastern University. My Department integrates degree granting programs at the Bachelor's,
28 Master's and Doctorate level, and includes emerging subjects of interest in global regulatory

1 affairs. In this position I lead the development of a new undergraduate advanced engineering
2 degree program in mechatronics, administrative and curricular revision of several existing
3 degree programs to ensure smooth transition into higher level credentials, as well as several
4 certificate programs at both the undergraduate and graduate levels. I also lead strategic
5 development and tactical execution of operations relevant to the portfolio, including ensuring
6 industry alignment, curriculum development, budget management, global marketing and
7 enrollment management, faculty capacity planning, fund-raising, accreditation and licensure. I
8 served as Chair of the CPS Faculty Review and Promotions Committee (FRPC) (AY19-20),
9 Northeastern University Faculty Senate Financial Affairs Committee (FAC) (AY19-20); and
10 provided leadership and support for setup and administration of COVID-19 campus-based
11 diagnostics testing. I am an ad Hoc FDA Reviewer on Orthopedic Devices and Implants
12 Committee, Review Member, 2018 Congressionally Directed Medical Research Program
13 (CDMRP), 2019 Psychological Health and Traumatic Brain Injury (TBI) Research Program,
14 2019 Joint Warfighter Medical Research Program (JWMRP), Grant Review, and FDA
15 associated Cancer Prevention and Research Institute of Texas Product Development Grant
16 Review Panels (CPRIT PDEV) from 2020 to 2024.

- 17 7. I am heavily involved with the Regulatory Affairs Professional Society (RAPS), which is a
18 preeminent, global professional association for regulatory professionals in the healthcare and
19 medical device industries. I hold a certification in regulatory affairs from RAPS. I served on the
20 RAPS Board of Directors from July 2015 to June 2016. Since 2010, I have been a Bioscience
21 Regulatory Affairs Consultant for RAPS. In this role, I have assisted with restructuring
22 Regulatory Affairs Certification (RAC) exams, from geographically based (i.e. US vs EU) to
23 product-based exams (i.e. Medical Devices vs Pharmaceuticals). I also coauthored development
24 of medical device quality systems online course - Quality System Regulations (QSRs), co-
25 authored development two levels of supply chain management courses, and co-authored course
26 in international medical device regulations for China, Japan, Singapore and South Korea, with
27 a specific focus on Singaporean regulations. I was also previously President of the Board of
28 Directors for the Medical Development Group of Boston from June 2014 to June 2016.

- 1 8. Additionally, I have an established record of consistent productivity and success with direct
2 FDA and global regulatory interactions and negotiations, including Type A, B & C meetings
3 with FDA. My list of regulatory team led/supported accomplishments include filing of 38
4 investigational device exemptions (IDE), 40 510(k) premarket notifications, 14 medical device
5 premarket approval applications (PMA), 23 investigational new drug applications (IND), and
6 13 new drug applications/biologics license applications (NDA/BLA) in the US. The breadth &
7 depth of my experience also includes successful interactions with EU notified bodies and the
8 EMA, and 10+ years of direct interaction with the Brazilian ANVISA, Japanese Ministry of
9 Health, Labor and Welfare (MHLW) and Chinese Food and Drug Administration (CFDA)
10 organizations.
- 11 9. Moreover, I am skilled in working with other global healthcare market space stakeholders to
12 evaluate, develop and execute biomedical product regulatory. As of December 2023,
13 biomedical product and associated services launches I have managed or supported in such areas
14 as orthopedics, biologics, women's health, infectious disease, molecular diagnostics and rare
15 disease spaces have generated over \$27.0 B in global revenue.
- 16 10. In addition, I have specialized in writing and submitting medical device IDE's, 510(k)
17 premarket notifications, de novo 510(k's) and Premarket Approval Applications (PMA's) for
18 various intended uses including human papillomavirus (HPV), hepatitis C (HepC), and hepatitis
19 B (hepB) diagnostic testing, as well as interventional cardiology, cardio-thoracic, orthopedic,
20 general surgery, urology, women's health, and spinal disease indications. I am experienced in
21 the global regulatory aspects of gene therapy based therapeutic approaches in several disease
22 states including Duchenne Muscular Dystrophy (DMD), hemophilia & oncology. I have worked
23 extensively with and taught China Food and Drug Administration (CFDA) inspectors and
24 companies in both China and the US, as well as Indian companies and Drugs Controller General
25 of India officials in India with respect to US regulations for biomedical product market
26 approvals. I have conducted primary market research with regard to clinical, regulatory and
27 reimbursement/market access requirements. I developed US regulatory strategies for biological
28 scaffold based orthopedic ligament repair products. I worked with two prominent international

1 Universities, located in Australia and China, to evaluate the US regulatory and reimbursement
2 environments for collagen-based orthopedics and biologics related technologies to the US
3 market.

4 11. I have been working in the biomedical products industry as an employee of several
5 manufacturing organizations including Siemens Healthcare, Smith & Nephew, Anika
6 Therapeutics, and Cardinal Health over the past 25 years. I have also served as a frequent
7 contributor and consultant to the medical device industry on a wide variety of topics including
8 global regulatory submissions, product design, quality management systems & assurance, and
9 reimbursement issues.

10 12. At Smith & Nephew, which is a \$4.5 B global developer, marketer and manufacturer operative
11 endoscopic and orthopedic products and procedures, I held various titles and responsibilities,
12 which included leading regulatory affairs and clinical development integration of a \$325M
13 biomaterials and cartilage repair company.

14 13. I was an ad Hoc Reviewer for the Journal of Immunology and the Journal of Experimental
15 Medicine. I have edited and/or written three chapters for a volume entitled Regulatory Affairs
16 for Biomaterials and Medical Devices published by Elsevier Publishing in July 2014. Since
17 1996, I have been an Editor of the International Journal of Cell Science, which is an
18 internationally, peer reviewed scientific journal known for rapid dissemination of high-quality
19 research in Cell Science. Similarly, since 2016, I have been an Editor of the Genomics & Gene
20 Therapy International Journal (GGTIJ). This Journal is specifically designed to provide
21 researchers around the world with the most recent topics pertaining to genetics and new gene
22 therapies. I have published close to thirty peer-reviewed articles on various regulatory topics,
23 including a publication on overcoming the challenges in getting cancer vaccines to market.

24 14. In sum, I have decades of experience in the regulation of the healthcare industry. I currently
25 work as a consultant to pharmaceutical companies on regulatory matters, including consulting
26 on submissions to the FDA related to pharmaceutical products and labeling. I have also
27 consulted with pharmaceutical companies on vaccines, including consulting on the design of
28 clinical trials for vaccines. I have managed an HPV genotyping platform and consulted with

1 pharmaceutical companies regarding the development of vaccines and diagnostic assays
2 targeting HPV. I have served as a consultant to the FDA, contributed to FDA panels, and have
3 met with FDA personnel regarding development of pharmaceutical products. I have led and/or
4 supported dozens of complex FDA submissions, including investigational new drug
5 applications, new drug applications, and biologics license applications.
6

7 SUMMARY OF METHODOLOGY

8

- 9 15. To evaluate the questions presented to me regarding the Gardasil and Gardasil 9 labeling
10 including Warnings, I applied federal statutes, regulations, and FDA guidance to the evidence.
11 I used my experience, training, and education in pharmaceutical regulatory affairs, including
12 my work consulting with the FDA.
- 13 16. More specifically with regard to my evaluation of the evidence regarding Merck's Warning
14 obligations, I applied 21 C.F.R. § 201.57(c)(6)(i), 21 C.F.R. § 601.12(f), the FDA Guidance
15 for Industry on Warnings and Precautions, Contraindications, and Boxed Warning Sections of
16 Labeling for Human Prescription Drug and Biological Products (October 2011) and FDA
17 Review of Vaccine Labeling Requirements For Warnings, Use Instructions, and Precautionary
18 Information, Sept 2004 Guidance, among others as listed in my Report.
- 19 17. This regulation requires that a drug and/or vaccine manufacturer add a Warning about any
20 "clinically significant hazard" associated with product "as soon as there is reasonable evidence
21 of a causal association" and, importantly, "a causal relationship need not have been definitely
22 established."¹ The FDA has explained that "causal association" in this context only means that
23 "at least a reasonably plausible causal relationship must exist." 65 Fed. Reg. 81082-01, 81094
24 (Dec. 22, 2000). I applied this standard to my review of Merck internal documents, clinical trial
25 records, pre-clinical trial records, adverse event reports, deposition transcripts, and published
26 medical literature. Particularly with the review of corporate witness deposition transcripts of
27

28 ¹ Discussed on pages 14-18 of Ex. 1.

1 Merck current and former employees, such as Bernhard Heiles, Veronica Urdaneta, Mary Ann
2 Goss, and Alison Fisher. As Merck’s own regulatory expert Dr. David Feigal has correctly
3 noted, whether the threshold of “reasonable evidence of a causal association” has been crossed
4 comes down to a “scientific judgment call.”²

5 18. Also, in evaluating the adequacy of Merck’s pharmacovigilance plan, I utilized the applicable
6 regulations.³

7 19. In evaluating Merck’s marketing of Gardasil, I applied 21 C.F.R. § 312.7, which prohibits
8 manufacturers from promoting an investigational product as safe or effective, and 21 C.F.R. §
9 202.1, which requires—among other things—that manufacturers’ prescription drug
10 advertisements not be false or misleading and that they “present a fair balance between
11 information relating to side effects and contraindications and information relating to
12 effectiveness of the drug.” I applied these regulations in reviewing Merck’s marketing materials
13 and Merck’s correspondence with the FDA’s Advertising & Promotional Labeling Branch.⁴

14 20. Finally, in evaluating whether or not Merck failed to list HPV L1 protein DNA fragments as an
15 ingredient in the Gardasil label, I applied 21 C.F.R. §§ 201.57, 610.61, which requires
16 ingredients to be listed in package inserts, to my review of Gardasil labels and Merck documents
17 indicating that Gardasil does, in fact, contain HPV L1 protein DNA fragments.⁵

18
19 **SUMMARY OF OPINIONS**

20
21 **A. Labeling Opinions**

22
23 ² Ex. 2: Feigal Dep. at 10:16-17.

24 ³ See, e.g., 21 C.F.R. § 314.80 (manufacturers “must ... develop written procedures for the surveillance,
25 receipt, evaluation, and reporting of postmarketing adverse drug experiences to FDA.” That
26 surveillance must include “review of all adverse drug experience information obtained or otherwise
27 received by the applicant from any source, foreign or domestic, including information derived from
28 commercial marketing experience, postmarketing clinical investigations, postmarketing
epidemiological/surveillance studies, reports in the scientific literature, and unpublished scientific
papers. ...”). See also 21 C.F.R. § 600.80.

⁴ Discussed on pages 45-54 of Ex. 1.

⁵ Discussed on pages 61-64 of Ex. 1.

1 21. Following my review of the Gardasil labels, it is my opinion that throughout the lifecycle of the
2 product, non specific POTS-like symptoms were added as adverse reactions, rather than
3 including a Warning of the autoimmune syndrome. For example, in July 2006, nausea and
4 dizziness were added to Table 6 for Common Adverse Reactions for “Vaccine related Injection-
5 site and Systemic Adverse Experiences”. In April 2007, various symptoms were added to the
6 “post-marketing reports” section in the label that include: dizziness and syncope. In December
7 2007, the “post-marketing reports” section in the label was updated to include arthralgia,
8 myalgia, asthenia, fatigue, and malaise. In September 2008, there was a new Package Insert
9 format. In this update, the “post-marketing reports” section in the label was updated to include
10 autoimmune hemolytic anemia, autoimmune diseases, motor neuron disease, paralysis,
11 seizures, syncope sometimes resulting in falling with injury, transverse myelitis, among others.
12 The December 2008 label was updated to add chills to the “post-marketing reports” section. In
13 May 2009, syncope was elevated from an “adverse reaction” to a Warning in Section 5 of the
14 label by FDA mandate. Syncope is one of the symptoms of the POTS constellation. In the years
15 that followed this labeling change, Merck continued to add other symptoms of POTS to
16 postmarketing sections of its labels, but never a Warning of POTS; rather Merck merely added
17 what appeared to be a random collection of symptoms without ever connecting them to one
18 another. The “post-marketing reports” section in the label was updated to state, “syncope
19 including convulsive syncope (tonic-clonic movements and other seizure-like activity)
20 sometimes resulting in falling with injury” (additions in bold). Convulsive syncope was
21 removed from the June 2009 label. In October 2009, acute disseminated encephalomyelitis was
22 added to the “Post-marketing Reports” in Adverse Reactions section.

23 22. Taken together, autoimmune events and POTS-like symptoms were gradually added for many
24 years in the Gardasil label. However, **these additions were not Warning.** Indeed, the FDA
25 Guidance for Industry on Warnings and Precautions, Contraindications, and Boxed Warning
26 Sections of Labeling for Human Prescription Drug and Biological Products (October 2011)
27 states that the Warnings section 5 should include “a succinct description of the adverse events
28 and outcome” - including “significant sequelae”. Section 6 listing of adverse reactions in a

1 product label are not presented as a Warning (which would be in Section 5) and do not amount
2 to a Warning.

3 23. It was possible—indeed required by applicable regulations⁶—for Merck, without prior FDA
4 approval, to have explicitly provided a Warning of the risks of autoimmune reactions, including
5 POTS, from Gardasil administration by January 2011.

6 24. By January 2011, Merck did know, or should have known, there is reasonable evidence of a
7 causal association between Gardasil and autoimmune reactions, including development of
8 POTS. Such knowledge derives from various sources, including:

9 a. **Aluminum Adjuvant in Gardasil.** Adjuvants are substances added to vaccines to
10 enhance the body’s immune response. Gardasil contains Merck’s proprietary aluminum-
11 containing adjuvant, AAHS. It is accepted in the medical community that aluminum-
12 based adjuvants can induce autoimmune disease.⁷

13 b. **HPV L1 Protein DNA in Gardasil.** Merck has acknowledged that Gardasil contains
14 HPV L1 DNA fragments and that such DNA is a Toll Like Receptor 9 (TLR 9) agonist
15 that stimulates an immune response. Thus, HPV L1 protein DNA operates as an
16 additional adjuvant in Gardasil. However, HPV L1 DNA is not a listed ingredient on the
17 Gardasil label, and it does not appear that Merck has ever measured how much HPV L1
18 DNA is injected into Gardasil recipients.⁸

19 c. **Animal Studies:** Merck’s pre-clinical animal trials that showed “[t]reatment-related
20 enlargement of iliac lymph nodes” in mice; while these symptoms warranted additional
21 investigation of autoimmune reactions, Merck failed to test for further evidence of
22 autoimmune disorders in the pre-clinical setting.⁹

23
24 ⁶ See 21 C.F.R. §§ 201.57(c)(6), 314.70(c)(6), 601.12(f)(2).

25 ⁷ Discussed at pages 54-57 of Ex. 1 (quoting Ex. 3: Petrovsky, *Freeing vaccine adjuvants from*
26 *dangerous immunological dogma*, 7 EXPERT REV. OF VACCINES 7-10 (2008)).

27 ⁸ Discussed at pages 61-64 of Ex. 1. Merck never listed HPV L1 DNA fragments on the label for
28 Gardasil; Merck has not attempted to quantify the HPV L1 DNA fragments present in Gardasil. Such
fragments can act as an adjuvant, increasing Gardasil’s immunogenicity, and the healthcare community
should have been warned. Merck’s failure to list HPV L1 DNA fragments violated federal labeling
standards. See 21 C.F.R. §§ 201.57, 610.61 (requiring ingredients to be listed in package inserts).

⁹ Discussed at pages 65-66 of Ex. 1 (citing Ex. 4: MRKGAR04197803).

1 d. **Clinical Trials:** Merck’s pre-licensure clinical trials were generally not designed to
2 detect autoimmune events in human subjects because the study designs were too short
3 to capture the time that is needed for manifestation and detection of latent,
4 heterogeneous autoimmune injuries caused by vaccines such as POTS.¹⁰ However, to
5 the extent that evidence of auto-immune reactions were occurring, that evidence could
6 be masked by Merck’s use of AAHS (an active adjuvant ingredient) as its “placebo”
7 comparator.¹¹ In my opinion, the use of an aluminum adjuvant as a “placebo” was
8 improper clinical trial practice for this vaccine. Also, symptoms of auto-immune
9 reactions were often recorded as “new medical history,” with little detail, rather than as
10 adverse events.¹² With these vaccine trials, this was also an improper clinical trial
11 practice that would further mask any auto-immune evidence. Nonetheless, symptoms of
12 POTS did occur within the study duration of the Gardasil/Gardasil 9 clinical trials. For
13 example:

- 14 i. Patient AN10593 was diagnosed with dysautonomia in 2008 following her last
15 Gardasil 9 injection. POTS is a form of dysautonomia.¹³
- 16 ii. Patient AN29076 was diagnosed with syncope, headache, and POTS after her
17 first vaccination in 2010.¹⁴
- 18 iii. Patient AN37083 was hospitalized with syncope in December 2010 only 13 days
19 after her second dose of Gardasil 9 and later diagnosed with dysautonomia.¹⁵
- 20 iv. Patient AN37803 experienced POTS five days after her second dose of Gardasil
21 9 in October 2010.¹⁶

22 ¹⁰ Discussed at page 67 of Ex. 1.

23 ¹¹ Discussed at pages 55-57, 140 of Ex. 1.

24 ¹² Discussed at pages 69-61 of Ex. 1.

25 ¹³ Discussed at page 68 of Ex. 1. *See also* Ex. 5: Blitshteyn et al., *Autonomic dysfunction and HPV*
26 *immunization-an overview*, IMMUNOL RES. (2018) (“dysautonomia is sometimes used as an umbrella
27 term that includes all autonomic disorders, ... [including] postural orthostatic tachycardia syndrome
28 (POTS)”).

¹⁴ Discussed at page 68 of Ex. 1.

¹⁵ Discussed at page 69 of Ex. 1 (citing Ex. 6: MRKGAR06725988; Ex. 7: MRKGARE00033608).

¹⁶ Discussed at page 70 of Ex. 1 (citing Ex. 8: MRKGAR00565819; and Ex. 9: Dep. of Alison Fisher
on May 16, 2024 at 306:14-19).

- 1 v. Patient AN71508 began experiencing symptoms in January 2010 that included
2 syncope, dizziness, nausea, headache, tiredness, and low muscle strength and
3 was later diagnosed with POTS. However, Merck misrepresented the onset date
4 as November 2013 in a submission to the FDA.¹⁷
- 5 vi. Patient AN71686 developed headache, nausea, and orthostatic intolerance in
6 October 2009 after her second dose of Gardasil and was later diagnosed with
7 POTS.¹⁸
- 8 e. Merck's failure to properly conduct and analyze its clinical trials was significant from a
9 regulatory perspective because whether it was possible to add a warning to a prescription
10 drug label hinges not only on what information the manufacturer had but also the
11 information the manufacturer should have had. If Merck had properly analyzed its
12 clinical trial data, reasonable evidence of a causal association with autoimmune
13 disorders, including POTS, likely would have been demonstrated by the clinical trial
14 data. Indeed, evidence of a causal association that was gathered during post marketing
15 surveillance, discussed below, is the type of evidence that could have and should have
16 been gathered, with additional detail, during Merck's clinical trials.
- 17 f. **Post marketing adverse event reports of POTS, POTS symptoms, and autoimmune**
18 **disease:** Following the release of Gardasil on the market in the United States in 2006,
19 post marketing evidence of Gardasil's potential to cause autoimmune disease, including
20 POTS, continued to accumulate. For example:
- 21 i. A 2006 Merck report listed an overwhelming number of subjects with separate
22 POTS-like symptoms, such as headache, nausea, syncope, dizziness, and
23 fatigue.¹⁹
- 24 ii. Merck received a 2007 report of a 21-year-old female who developed serious
25

26 ¹⁷ Discussed on page 71 of Ex. 1 (citing Ex. 10: MRKGAR_E00022250; Ex. 11: MRKGAR06392417;
and Ex. 12: MRKGAR01020181).

27 ¹⁸ Discussed on page 75 of Ex. 1 (citing Ex. 13: MRKGARE00022255; Ex. 14: MRKGAR00082652 -
V503 Protocol 001 Clinical Study Report at pgs. 4658; 4879).

28 ¹⁹ Discussed on page 80 of Ex. 1 (citing Ex. 15: MRKGAR00617299).

- 1 POTS with symptom onset coinciding with first Gardasil injection.²⁰
- 2 iii. Merck received a 2007 report of unresolved POTS following Gardasil
- 3 vaccination.²¹
- 4 iv. By June 2008, Merck had received 37 serious reports of muscular weakness in
- 5 Gardasil recipients.²²
- 6 v. Merck received a 2008 report of a 14-year-old experiencing weakness
- 7 (potentially terminal) following Gardasil vaccination, with a differential
- 8 diagnosis that included “autoimmune polyneuropathy.”²³
- 9 vi. Merck also received a 2009 report of 15-year-old female who developed POTS
- 10 following at least two doses of Gardasil.²⁴
- 11 vii. Merck received a 2010 report of “serious” POTS following Gardasil vaccination,
- 12 with onset date listed as December 2006.²⁵
- 13 viii. In April 2010, a 12-year-old Gardasil 9 clinical trial participant was diagnosed
- 14 with POTS 24 days after her first injection. Merck instructed its investigators to
- 15 characterize the patient’s POTS as “new medical history” rather than as an
- 16 adverse reaction. As a result, less detail was collected by Merck, and Merck’s
- 17 ability to assess the event for causality was limited.²⁶
- 18 ix. Merck was in receipt of at least four additional POTS reports by January 2011,
- 19 three of which were listed as “serious”.²⁷

20 ²⁰ Discussed on pages 80-81 of Ex. 1 (citing Ex. 16: MRKGAR00624984; Ex. 17: MRKGAR04746526).

21 ²¹ Discussed on page 80 of Ex. 1 (citing Ex. 18: MRKGAR10500188).

22 ²² Discussed on page 82 of Ex. 1 (citing Ex. 19: MRKGAR04754727; Ex. 20: MRKGAR04754729; Ex. 21: MRKGAR04754766).

23 ²³ Discussed on pages 83-84 of Ex. 1 (citing Ex. 22: MRKGAR09342284; Ex. 23: MRKGAR09342286; Ex. 24: MRKGAR09342288).

24 ²⁴ Discussed on page 84 of Ex. 1 (citing Ex. 25: MRKGAR04787615; Ex. 26: MRKGAR04806065).

25 ²⁵ Discussed on page 85 of Ex. 1 (citing Ex. 27: MRKGAR04741097).

26 ²⁶ Discussed on page 85 of Ex. 1 (citing Ex. 28: MRKGAR04729449; Ex. 29: MRKGAR_E00038512).

27 ²⁷ Discussed on pages 85-86 of Ex. 1 (citing Ex. 30: MRKGAR00617559 at MRKGAR00617843-4 (15-year-old female diagnosed with POTS, onset listed as July 2009); *id.* at MRKGAR00617876-7 (13-year-old female diagnosed with POTS, onset listed as September 2009); Ex. 31: MRKGAR03460302 at MRKGAR03460428-9 (patient 1991007USA01550 diagnosed with POTS); Ex. 32:

28

1 g. In 2012, Merck started using the “STAR” system for post-market surveillance
2 monitoring. That system quantified adverse events with an “EB05” score. An EB05 of
3 greater than 1 indicates that the adverse event is occurring at higher-than-expected
4 ratios.²⁸ The EB05 for POTS consistently indicated a safety signal (2.383 in June 2012;
5 2.483 in September 2013; 2.823 in December 2013; 2.847 in March 2014; 2.866 in
6 September 2014; 3.612 in September 2017; 3.621 in December 2017; 3.719 in
7 December 2020).²⁹ The elevated EB05 signal for POTS provides additional support that
8 there is reasonable evidence of a causal association; Merck could have and should have
9 performed these disproportionality analyses from the start of its post marketing
10 surveillance.

11 h. **Published literature:** Published literature has established that there is reasonable
12 evidence of a causal association between Gardasil vaccination and autoimmune
13 reactions, including POTS. Although my opinion is that Merck’s obligation to warn of
14 autoimmune conditions, including POTS, was triggered by January 2011, the published
15 literature both before and after that time illustrates the sorts of information that was
16 available to Merck prior to January 2011 if Merck had chosen to collect, examine, and
17 analyze the data properly.

18 i. Medical literature has established that POTS often has an autoimmune
19 etiology.³⁰

20 ii. A pivotal case report published in the European Journal of Neurology described

21 MRKGAR05851385 at MRKGAR05851584 (18-year-old female diagnosed with POTS, onset listed
22 as January 2010)). Merck has also received additional reports of POTS in Gardasil recipients; however,
23 many of these cases are missing detail, and it does not appear that Merck performed a causality
24 assessment. *See* Ex. 1 at 89-90 (discussing additional POTS reports).

25 ²⁸ Discussed on page 86 of Ex. 1 (citing Ex. 33: MRKGAR01043964).

26 ²⁹ Discussed on pages 86-91 of Ex. 1 (citing various Merck documents).

27 ³⁰ Discussed on page 64-65 of Ex. 1 (citing Ex. 34: Thieben et al., *Postural orthostatic tachycardia*
28 *syndrome: the Mayo clinic experience*, MAYO CLINIC PROCEEDINGS (2007) (“findings suggest a
neuropathic basis for at least half of the cases of POTS and that a substantial percentage of cases may
be autoimmune”); Ex. 35: Kasmani, *Postural Orthostatic Tachycardia Syndrome Associated with*
Mycoplasma pneumoniae, INFECTIOUS DISEASE IN CLINICAL PRACTICE (2009) (POTS is associated with
autoimmunity). Indeed, even Merck has acknowledged the potential autoimmune origins of POTS. *See*
Ex. 36: MRKGAR01156409; Ex. 37: MRKGAR12480601.

1 a 20-year-old woman who developed POTS two weeks after her first Gardasil
2 dose, showing a significant increase in heart rate during tilt table testing
3 (Blitshteyn, 2010).³¹

4 iii. In 2011, Chao et al. published a Merck-funded and Merck co-authored study
5 aimed at evaluating autoimmune reactions from Gardasil. Despite the short
6 duration, and the authors' acknowledgment that it was under-powered to assess
7 for many autoimmune reactions, the study indicated a significantly significant
8 increased rate of Hashimoto's disease among Gardasil recipients.³² Thus, even
9 Merck's own study provides evidence that Gardasil has a causal association with
10 autoimmune reactions.

11 iv. In 2014, Tomljenovic et al. published a case report detailing a 14-year-old girl
12 who developed POTS and chronic fatigue syndrome following her second dose
13 of the Gardasil vaccine. This case was notable for positive autoantibody tests,
14 suggesting an autoimmune response triggered by the vaccination (Tomljenovic
15 et al., 2014). The authors concluded that a thorough investigation into the
16 association between Gardasil and POTS was warranted due to the temporal
17 relationship and the autoimmune findings.³³

18 v. In 2015, Brinth published a series of studies aimed at evaluating adverse
19 reactions associated with Gardasil. The Brinth studies indicate that studied
20 individuals who experienced side-effects after Gardasil vaccination experienced
21 high rates of POTS and POTS symptoms (orthostatic intolerance, headache,
22
23

24 ³¹ Discussed on page 85, 98 of Ex. 1 (citing Ex. 38: Blitshteyn, *Postural tachycardia syndrome after*
25 *vaccination with Gardasil*, EUR. J. OF NEUROLOGY (2010)).

26 ³² Discussed on pages 108-110 of Ex. 1 (citing Ex. 39: Chao, *Surveillance of autoimmune conditions*
27 *following routine use of quadrivalent human papillomavirus vaccine*, J. OF INTERNAL MED. (2011)).

28 ³³ Discussed on pages 98-99 of Ex. 1 (citing Ex. 40: Tomljenovic, *Postural Orthostatic Tachycardia*
with Chronic Fatigue After HPV Vaccination as Part of the "Autoimmune/Auto-inflammatory
Syndrome Induced by Adjuvants": Case Report and Literature Review, J. OF INVESTIGATIVE MED. HIGH
IMPACT CASE REPORTS (2014)).

1 fatigue, cognitive dysfunction).³⁴

2 vi. In 2017, Schofield et al. published a case report of an 11-year-old girl who
3 developed severe autonomic neuropathy, including POTS, after vaccination with
4 Gardasil. The case improved with immune therapy, suggesting an immune-
5 mediated reaction.³⁵

6 vii. A case series by Blitshteyn (2014) examined six previously healthy young
7 women who developed new-onset POTS shortly (6 days to 2 months) after
8 receiving Gardasil. The temporal proximity of vaccination to the onset of
9 symptoms provides evidence of a causal association. The authors called for
10 increased awareness among healthcare providers regarding the possibility of
11 POTS following HPV vaccination.³⁶

12 25. While there are various permutations of particular language that could have satisfied Merck's
13 warning obligations as to autoimmunity and POTS, it is my opinion that, by January 2011,
14 Merck should have included a Warning in the WARNINGS AND PRECAUTIONS section of
15 the Gardasil label. The following is an example of such a Warning that could have satisfied
16 Merck's warning obligation under FDA regulations:

17 Section 5 WARNINGS AND PRECAUTIONS

18 5.3 Serious adverse events can occur following the administration of GARDASIL.
19 Gardasil may cause persistent headaches, fatigue, presyncope, tachycardia,
20 gastrointestinal symptoms, and/or limb pain or weakness. This constellation of
21 symptoms may relate to autoimmune conditions, such as postural orthostatic
22 tachycardia syndrome (POTS). Careful history of any individual should be gathered
before vaccination and if these symptoms present following vaccination, further doses
should be avoided, and the patient should be referred for evaluation of autoimmune
disease.

23 ³⁴ Discussed on pages 101-104 of Ex. 1 (citing Ex. 41: Brinth, *Suspected side effects to the quadrivalent*
24 *human papilloma vaccine*, DANISH MED. J. (Apr. 2015); Ex. 42: Brinth, *Is chronic fatigue*
25 *syndrome/myalgic encephalomyelitis a relevant diagnosis in patients with suspected side effects to*
26 *human papilloma virus vaccine*, 1 INT. J. OF VACCINE & VACCINATION 3 (2015); Ex. 43: Brinth,
Orthostatic intolerance and postural tachycardia syndrome as suspected adverse effects of vaccination
against human papilloma virus, 33 VACCINE 2602 (2015)).

27 ³⁵ Discussed on pages 98-99 of Ex. 1 (citing Ex. 44: Schofield et al., *Autoimmunity, Autonomic*
Neuropathy, and HPV Vaccination, A Vulnerable Subpopulation, CLINICAL PEDIATRICS (2017)).

28 ³⁶ Discussed on page 100 of Ex. 1 (citing Ex. 45: Blitshteyn, *Postural Tachycardia Syndrome Following*
Human Papillomavirus Vaccination, 21 EUR. J. OF NEUROLOGY 135 (2014)).

1 **B. Marketing Opinion**

2 26. Applying the FDA’s Advertising & Promotional Labeling Branch (“APLB”),³⁷ which regulates
3 advertising and promotion of pharmaceutical products to ensure the marketing is truthful,
4 accurate, science-based, non-misleading and balanced in compliance with federal laws and
5 regulations. I reviewed internal Merck marketing and strategy documents,³⁸ and correspondence
6 concerning Gardasil advertisements.

7 27. Based on that review pursuant to applicable regulations³⁹ it is my opinion, that Merck repeatedly
8 misrepresented the efficacy of Gardasil and misled consumers and physicians regarding
9 Gardasil’s ability to supplant screening (Pap smears) and prevent all types of cervical and anal
10 cancer, in violation of federal marketing standards. It is also my opinion that Merck’s aggressive
11 and misleading marketing of Gardasil was driven by its initiative to grow a multi-billion-dollar
12 market for Gardasil through unconventional methods,⁴⁰ including direct-to-consumer
13 advertising and media outreach with celebrities.⁴¹

14
15 **C. Pharmacovigilance Opinion**

16 28. Merck’s pharmacovigilance plan for Gardasil states its purpose to “pre-empt and guard against
17 erroneous associations that are made by anti-vaccine advocates” without mentioning that the
18 true purpose of pharmacovigilance is to ensure the safety of those vaccinated with Gardasil and
19 Merck’s documents show that it resisted additional post marketing surveillance studies,
20 reducing the pool of available risk information about Gardasil.⁴² However, the FDA has
21 emphasized the purpose of pharmacovigilance: “evaluating and characterizing a product’s risk

22 ³⁷ Discussed on pages 50-54 of Ex. 1 (citing Ex. 46: MRKGAR08414859; Ex. 47: MRKGAR08324087;
23 Ex. 48: MRKGAR08298004; Ex. 49: MRKGAR14195675; Ex. 50: MRKGAR15000576; Ex. 51:
24 MRKGAR08324195; and Ex. 52: MRKGAR15000574).

25 ³⁸ Discussed on pages 46-49 of Ex. 1 (citing Ex. 53: MRKGAR04381650; Ex. 54: MRKGAR03923556;
26 and Ex. 55: MRKGAR00612209).

27 ³⁹ See, e.g., 21 C.F.R. §§ 202.1, 312.7.

28 ⁴⁰ Merck’s profit motive in marketing Gardasil and its aggressive outreach strategies are discussed on
29 pages 49 to 50 of Ex. 1 (citing Ex. 56: MRKGAR03921182; Ex. 57: MRKGAR15229287; Ex. 58:
30 MRKGAR_R00085654; and Ex. 59: MRKGAR08233606).

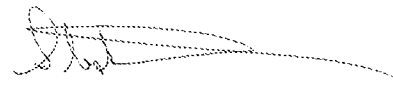
31 ⁴¹ My review of Merck’s marketing strategy of Gardasil is discussed on pages 45-54 of Ex. 1.

32 ⁴² Discussed on page 57 of Ex. 1 (citing Ex. 60: MRKGAR03462607).

1 profile and ... making informed decisions on risk minimization.” Thus, it is my opinion that
2 Merck’s pharmacovigilance plan did not satisfy FDA standards and emphasized profit over
3 safety.⁴³
4

5 I declare under penalty of perjury under the laws of the State of California that the foregoing is
6 true and correct, and that this declaration was executed on December 30, 2024 at Boston,
7 Massachusetts.
8
9
10

11 Dated: December 30, 2024


12 Stephen F. Amato, Ph.D., M.B.A.
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28 ⁴³ Discussed on pages 57-59 of Ex. 1.

1 **PROOF OF SERVICE**

2 STATE OF CALIFORNIA, COUNTY OF LOS ANGELES.

3 I am employed in the county of Los Angeles, State of California. I am over the age of 18 and
4 not a party to the within action; my business address is: 11111 Santa Monica Blvd., Suite 1750, Los
5 Angeles, CA 90025.

6 On January 8, 2025, I served the following document(s): **AMENDED DECLARATION**
7 **OF STEPHEN AMATO, PhD, MBA** on the interested parties in this action by placing a true copy
thereof enclosed in sealed envelopes addressed as follows:

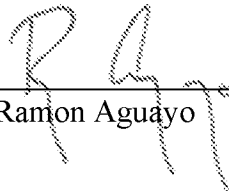
8 **BY MAIL:** I am readily familiar with the firm's practice of collection and processing
9 correspondence for mailing. Under that practice it would be deposited with the U.S. postal
10 service on that same day with postage thereon fully prepaid at Los Angeles, California in the
11 ordinary course of business. I am aware that on motion of the party served, service is presumed
invalid if postal cancellation date or postage meter date is more than one day after date of deposit
for mailing an affidavit. (*Chair, Judicial Council of California only*)

12 **BY ELECTRONIC TRANSMISSION:** I caused the foregoing document to be sent via
13 electronic mail via Case Anywhere service system in accordance with the November 9, 2017,
14 Order Authorizing Electronic Service governing Los Angeles Superior Court Case No.
BC628589.

15 **BY PERSONAL SERVICE:** I caused to be delivered such envelope by hand to the offices of
16 the addressee listed below.

17 I declare under penalty of perjury under the laws of the State of California that the above is true
and correct.

18 Executed on January 8, 2025 at Los Angeles, California.

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Ramon Aguayo