The sterility of extracts in skin prick testing reservoirs: A quality assurance initiative

To the Editor:

In an article from *The Journal of Allergy and Clinical Immunology: In Practice* published in November 2018, "Safety of multidose immunotherapy vials after routine use," Nath et al[1] demonstrated that there was no risk of organism contamination after using extract immunotherapy maintenance vials in routine clinical practice. Other studies have demonstrated sterility of allergen extracts over time in immunotherapy vials from the manufacturer.[2,3] However, there are no publicly available studies that investigate microbial growth in allergen skin prick testing (SPT) systems. SPT is used frequently to confirm clinical sensitivity to suspected allergens and to select aeroallergens included in immunotherapy prescriptions. Although there has never been a documented infection caused by SPT, ensuring the sterility of SPT systems is paramount to ensure patient safety and reliable SPT results.[4,5] Therefore, we conducted a quality assurance initiative to evaluate the sterility of extracts used in SPT over a period of 1 month. We also sought to assess the sterility of extracts stored in SPT reservoirs over a time period of 2 months, so long as the manufacturers' documented expiration date had not yet been reached.

An SPT system was prepared using supplies from HollisterStier Allergy containing 48 commercial extracts and 2 control solutions (Table I). We used this system for routine patient SPT for 1 month. Then, using an aseptic technique, 100 μL of each extract was injected into separate thioglycollate mediums for sterility testing. These cultures were incubated for 19 days at 37°C in a non–carbon dioxide-enriched incubator and examined daily for microbial growth. A separate SPT system was also prepared using the same supplies, extracts, and aseptic technique. However, this system remained unused for patient testing. At any time SPT was performed in our clinic, this tray was removed from refrigeration and transferred in tandem with a system being used for patient testing to subject it to similar temperatures. At the predetermined times of 1 and 2 months from the creation of this tray, 100 μL of extract from each reservoir was also separately cultured in thioglycollate medium.

No extracts from the SPT system used in routine patient testing over the course of 1 month demonstrated any organism growth. In the SPT system that remained unused for 2 months, but subject to similar temperature fluctuations as systems used for patient testing, cultures likewise failed to exhibit any organism growth.

We submit allergen extracts used in a common SPT system remaining free from bacterial growth over a prolonged period of time, further providing evidence for the safety of SPT. Our findings also suggest that it would be reasonable to schedule extract replacement in SPT reservoirs at intervals of every 2 months or when their respective expiration date is reached, as manufacturers only provide guidance by recommending replacing extracts in SPT systems "periodically."[6]

TABLE I. Aeroallergen extracts used in each SPT system

Reservoir no.	Extract	Concentration
1	Negative control 50% glycerin	50% glycerin
2	Alder, red	1:20 w/v
3	Ash, white	1:20 w/v
4	Birch mix	1:20 w/v
5	Box elder	1:20 w/v
6	Mabel, red	1:20 w/v
7	Cottonwood	1:20 w/v
8	Cypress, bald	1:40 w/v
9	Elm, Siberian	1:20 w/v
10	Hackberry	1:20 w/v
11	Mesquite	1:20 w/v
12	Mountain cedar	1:20 w/v
13	Mulberry, red	1:20 w/v
14	Oak mix	1:20 w/v
15	Olive, European	1:20 w/v
16	Palm, clean	1:20 w/v
17	Pecan	1:20 w/v
18	Sycamore	1:20 w/v
19	Walnut, black	1:20 w/v
20	Bahia	1:20 w/v
21	Bermuda	10,000 BAU/mL
22	Johnson	1:20 w/v
23	Rye, perennial	10,000 BAU/mL
24	Timothy	10,000 BAU/mL
25	Mites, F.	5000 AU/mL
26	Mites, P.	5000 AU/mL
27	Cat, standard	10,000 BAU/mL
28	Dog hair	1:100 w/v
29	Cockroach	1:20 w/v
30	Kochia	1:20 w/v
31	Cocklebur	1:20 w/v
32	Dock/Sorrel	1:20 w/v
33	Lambs quarters	1:20 w/v
34	Marshelder	1:20 w/v
35	Nettle	1:20 w/v
36	Pigweed	1:20 w/v
37	Plantain, english	1:20 w/v
38	Ragweed	1:20 w/v
39	Russian thistle	1:20 w/v
40	Sage/Mugwort	1:20 w/v
41	Alternaria	1:20 w/v
42	Aspergillus	1:20 w/v
43	Chaetomium	1:20 w/v
44	Drechslera	1:20 w/v
45	Epicardium	1:40 w/v
46	Fusarium mix	1:20 w/v
47	Helminthospor/Bipolaris	1:20 w/v
48	Hormodendrum/Cladosporium	1:20 w/v
49	Penicillium	1:20 w/v
50	Histamine positive control	10 mg/mL histamine dihydrochloride

AU, Allergy unit; *BAU,* bioequivalent allergy unit; *w/v,* weight/volume.
SPT systems were created using a ComforTen-Covered 60-Hole Tray, HollisterStier Skin Test Reservoirs, and either ComforTen skin test devices or Quintip devices.

These data provide the practicing allergist with more specific guidance than the manufacturers' recommendations.

Taylor J. Atchley, MD
Daniel A. Steigelman, MD
Sherry Trevino, MPH

Wilford Hall Ambulatory Surgical Center, Lackland AFB, Texas.

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Corresponding author: Taylor J. Atchley, MD, Wilford Hall Ambulatory Surgical Center, 1100 Wilford Hall Loop, Allergy and Immunizations Clinic, JBSA Lackland AFB, TX 78236. E-mail: taylor.j.atchley.mil@mail.mil.

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Reply

To the Editor:

Atchley et al[1] present further arguments supporting the safety and sterility of allergen extracts. As noted, multiple studies, to include our study, have demonstrated the sterility of allergen extracts over time.[2] We presented evidence that our current practice of administration of multidose vials adheres to patient safety standards as well as US Pharmaceutical General Chapter <797> Pharmaceutical compounding – Sterile Preparations (USP <797>). After routine use of mixed-aeroallergen extract maintenance vials, we found no risk of contamination and a lack of microbial growth 30 days past the 1-year manufacturer-recommended expiration date. Similarly, Atchley et al demonstrated the sterility of skin prick testing (SPT) systems used in routine patient testing. We believe the study presented by Atchley et al adds to the reservoir of data advocating for the sterility of allergen extracts by providing the practicing allergist with specific recommendations and reassurance about the use of SPT systems.

The United States Pharmacopeia released the final USP <797> standards on June 1, 2019. This revision details the personnel qualifications, appropriate facilities, and necessary documentation to continue in-office compounding of individual vial sets for allergen immunotherapy. These requirements allow allergists to compound extracts in an ISO Class 5 Primary Engineering Control (PEC) or in a dedicated Allergenic Extract Compounding Area (AECA). Most importantly, allergen extracts continue to be a separate section of the chapter. Previous studies have bolstered arguments in support of the standards set forth by the current USP<797> with regard to allergen extract vials. The data presented by Atchley et al are unique in that it validates the safety profile of allergy extracts, whether as multidose vials or used in SPT systems.

Priya I. Nath, MD, JD[a]
John F. Freiler, MD[b]
Robert A. Gomez, MT(ASCP)MBcm[c]

[a]Allergy and Immunizations Clinic, Langley Air Force Base Hospital, JB Langley-Eustis, Va
[b]Medical Readiness Agency, Air Force, JBSA Lackland AFB, Tex
[c]Allergy Research Laboratory, Wilford Hall Ambulatory Surgical Center, JBSA Lackland AFB, Tex.

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Corresponding author: Priya I. Nath, MD, JD, Allergy and Immunizations Clinic, Langley Air Force Base Hospital, 77 Nealy Avenue, JB Langley-Eustis, VA 23665. E-mail: Priya.i.nath.mil@mail.mil, nathpriya@gmail.com.

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