Glove permeation of chemicals: The state of the art of current practice, Part 1: Basics and the permeation standards

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Abstract

Skin exposure to chemicals in the workplace environment is a major concern, the hands being the major exposure sites. Employers purchase gloves that have permeation data generated from permeation "standards" of the American Society for Testing and Materials International (ASTM International), European Committee for Standardization (EN), and the International Organization for Standardization (ISO) that test pieces of glove material and allow a user-defined temperature. The relevant standards based on continuous contact are ASTM F739, ASTM D6978, EN 374, EN 16523, and ISO 6529. The aim was to analyze the current state of the scientific literature on glove permeation in the 21st century up to December 2018. The introduction sets out the background, objectives and rationale of the review and its methodology followed by presentation of basic glove chemical resistance terms and Fick's first law of diffusion, the details of the major permeation standards, their comparison, their critique, their research gaps; the scientific literature on whole glove permeation, and final conclusions. The major recommendation was to harmonize all the permeation standards and perform them at realistic work conditions, especially temperature. The whole glove system would be most useful for testing the thinnest gloves.

Keywords

ASTM F739; breakthrough times; dextrous robot hand; gloves; review; steady state permeation rates

Introduction

More than 10–15% of workers in the United States (U.S.) were estimated to risk potential exposure to chemicals via skin contact in 2013.[1] The Bureau of Labor and Statistics reported 18,500 cases (0.019% of total) of occupational dermal diseases in 2017 in the U.S., compared with 10,400 cases of respiratory diseases.[2] A 2017 report stated that skin diseases comprised 20–30% of occupational diseases in Europe.[3]

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In 2002, about 15 trillion pounds of chemicals were imported/produced in the U.S.,[4] and a peak of about 27 trillion pounds in 2005.[1,4] The U.S. chemical industry production index is an economic indicator that measures real output in weight, inflation-adjusted sales figures, or production worker-hours in the manufacturing, mining, electric and gas (but not construction) industries relative to the base year 2012. This index in 2002 was 85.1%; in 2005, 109.3%; in 2015, 97.3%; and in 2016, 98%.[5] Similar trends have been found in the European Union.[6] Many chemicals, but especially new ones, do not have standard analytical chemistry methods, and there are too many chemicals to test, as well as too many workers for individual testing.

Surprisingly, for such an important exposure route as skin, there are very few guidelines that might help define permissible exposures to chemicals and allow worker risk assessments. This lack of guidelines has probably also contributed to the relatively high incidence of skin disease. The major guidance system in the U.S. is based on a system of notations. Skin absorption that causes systemic effects for a chemical is currently notated as "skin"; dermal sensitization is "DSEN"; and animal skin/lung sensitization with little human data is "SEN" in the American Conference of Governmental Industrial Hygienists (ACGIH®) 2019 Threshold Limit Values (TLVs®) and Biological Exposure Indices (BEIs) booklet.[7] The National Institute for Occupational Safety and Health (NIOSH) has dermal guidelines[1] that incorporate skin irritation and skin absorption.[8] There is also a skin permeation calculator.[8] The Occupational Safety and Health Administration (OSHA) has skin notation nomenclature similar to ACGIH's 1968 recommendations, the major difference for "skin" being that the chemical is known to be dermally absorbed.[9] The United States (U.S.) Environmental Protection Agency (EPA) has strategies for estimating dermal exposure and the use of personal protective equipment (PPE).[10] The American Industrial Hygiene Association from 2008–2011 did have a Biological Environmental Exposure Level Project Team for skin risk assessment.[11] There is now a SkinPerm calculator.

Given the millions of employees potentially at risk in the world, more research and development are essential to anticipate, recognize, evaluate, control, and prevent skin exposures. Despite advances to prevent chemical exposures through the hierarchy of controls, gloves are still the primary hand protection for workers.[1] Often the hands are the first targets directly exposed to chemical, thermal, and mechanical hazards, often in combination.[1,2]

Gloves as a part of PPE are essential in both remediation/rescue/emergency operations for chemical spills, and to protect the hands during the work shift when chemicals are handled. A common directive in safety data sheets is to "Use the appropriate glove", something that has to be determined by a professional who needs to understand the factors involved and to employ "professional judgment." Part of the latter involves the application of past history to current practice. This suggested to the authors the need to analyze the current state of glove permeation.

The scientific research literature of glove permeation in the 21st century up to December 2018 was therefore searched and the results examined. The databases used were PubMed, the Hazardous Substances Data Bank (HSDB), Toxline (National Library of Medicine), and

Scifinder Scholar (Chemical Abstracts). All were searched with the words "glove permeation."

This article is divided into two portions. The current first portion covers the introduction, permeation basics, the past and existing permeation standards, their comparison, their scientific literature critiques in the form of scientific literature related to a whole glove model, and final conclusions. To obtain the relevant reference for this first portion, the general abstract set was refined with search words: ASTM F739, EN 374, ISO 6529, permeation cell, breakthrough time, steady state permeation, diffusion coefficient, theory, report, review, book, production, and manufacture. Duplicate citations were then eliminated before reading titles, abstracts and then if appropriate, the original source.

Glove permeation

The perfect glove would be inexpensive, resist the exposing chemical for as long as possible under workplace conditions, allow facile manipulation of work pieces, be comfortable, be reusable, and be recyclable.

Gloves used for handling of chemicals are designed to be chemically protective clothing (CPC) or disposable/single use. Thin gloves allow more facile manipulation of work pieces and greater wearer comfort than the thicker ones of the same material. For both types, the greater the thickness, the greater the chemical resistance, but manipulation of work pieces becomes more difficult, especially if they are small. For CPC gloves, a solution is to deposit multiple thin layers of different materials on the base material to produce "laminates" rather than double-glove. The usual solution with disposable gloves is to increase chemical resistance by choosing a thicker glove or by double gloving.

Gloves of the same material are also more resistant to chemicals if they are unsupported and unlined. The support and linings are often related to providing greater wearer comfort. Both features may cause leaks through stitchings, seams, and joins. Materials like cotton, wool, velvet, and synthetic blends are often used for supports and linings.

Glove resistance to chemicals can be assessed by glove degradation, penetration, and permeation and their permutations.[12–22]

- Degradation is the reaction of a chemical with the glove material that causes changes in glove physical/chemical properties, for example, swelling, shrinkage; color change; becoming harder or softer, stiffer, or brittle; texture deterioration; loss of elasticity, and loss of tensile strength.

- Penetration is the flow of bulk chemical through glove seams, gaps, holes, zippers, openings, closures, and material pretest microholes.[15,16] Molecular and/or mechanical change and/or hole formation in the glove may also cause challenge chemical penetration after exposure begins.[16]

- Permeation is the process by which a chemical moves through a material at the molecular level.[2,15–22] Permeation may occur without any observable effects on glove materials.[19,22] For a given glove material, permeation for different

chemicals varies and can occur rapidly or slowly.[22] Adsorption of the chemical occurs at the external surface followed by diffusion through the material (absorption), and then desorption from the opposite surface to a collection medium like air, liquid, or a solid like skin.[16,18] In the laboratory, the equipment to facilitate the permeation process is a permeation cell. The challenge chemical contacts the outer surface of a piece of glove material of thickness L and the collection medium contacts the inner surface. The challenge area of contact is usually the same as the collection area of contact. The analytical technique to assess what and how much is permeating must be appropriately accurate and precise. The permeation cells used in the permeation standards are described later.

Fick's first law of diffusion is used to describe chemical permeation.[14,19,20] (Eq. (1)):[19,20]

$$J = -D \times \frac{dc}{dx}, \tag{1}$$

where J is the permeation rate ($\mu g/cm^2/min$); c is the concentration of permeating chemical (the permeant) in the material ($\mu g/cm^3$) at x distance into the material from the outer surface (cm) so that dc/dx is the concentration gradient through the material of collection side area A and thickness L; D is the diffusion coefficient (cm^2/min). When dc/dx is constant, J is the steady state permeation rate (SSPR) and the time duration at the SSPR is the steady state period.

The J depends on parameters like: challenge chemical molecular size; solubility in the glove (the maximum absorbed weight of challenge chemical per gram of glove); analytical sensitivity; if the chemical is pure or a mixture; material L, A, texture; if forces are present that can deform the material to change L; and permeation cell size/geometry, temperature, collection side fluid flow rate, collection medium, and exposure duration/pattern. Such parameters also influence the time when the challenge chemical reaches a specified J and/or can be detected on the inner surface as denoted by a breakthrough time (BT). The SSPRs and BTs for the same chemical and nominal glove material from different manufacturers may also vary.[22]

Some researchers report the permeation rate in units of $\mu g/min$. This is actually the mass transfer rate or J multiplied by A. The units need to be noted.

Equation (1) can be integrated to Eq. (2):

$$J = -D \times \frac{C_1 - C_2}{L}, \tag{2}$$

where C_1 and C_2 are analyte concentrations at the outer surface and inner surface, respectively, when D is independent of the concentration gradient and L. At steady state, when J is constant and equal to the SSPR, C_1 for a pure permeating chemical is related to its solubility in the material (the latter also being assumed to be isotropic); and C_2 is zero when the collection medium is efficient. When C_2 is not zero, any measured J or SSPR is lower than when C_2 is zero.

Systems that involve recirculation or mass cumulation in the collection side are termed "closed-loop" as opposed to "open-loop" where there is no recirculation or mass cumulation.

Closed-loop collection allows application of Eq. (3) to define the diffusion coefficient D using lag time t_l :[19]

$$D = \frac{L^2}{6t_l}.$$

(3)

Lag time is measured by the linear extrapolation of the steady state period of the cumulated mass (concentration) or cumulated mass (concentration)/area permeation curve to the time axis.[19] Equation (3) assumes: (a) no significant (usually 10%) change in glove thickness; (b) no permeation at zero permeation time; (c) instant removal of permeated mass from the collection side surface into any collection medium; and (d) the rate of mass lost from the challenge side surface equals the collection side surface arrival/desorption rate in the steady state period.[19]

The mathematical model for non-Fickian diffusion is much more complex with D no longer simply related to L^2, but to variables related to materials being non-isotropic and the inner structure of each material.[20] This aspect will be dealt with more fully in the companion review.

Permeation standards

Permeation standards are protocols that describe the primary methods to determine glove permeation resistance.[21] Glove manufacturers use these protocols to test pieces of their materials. Most scientific researchers in this field use them as "gold standards" and/or in their actual research. These standards are used to measure the combined effects of penetration, degradation, and permeation. To interpret the data via Fick's first law requires no degradation and penetration. The standards require that preliminary degradation and penetration testing occur before permeation testing. The standards involve continuous (rather than intermittent) contact of a challenge chemical with a piece of the glove material, but not a whole glove. Consideration of the intermittent contact standards is beyond the scope of this article.

Several entities have developed these standards. The main organizations are the American Society of Testing and Materials (ASTM, now ASTM International) in the U.S.; the International Organization for Standardization (ISO) in Switzerland; and the European Union through its European Center for Standardization (CEN) and its current EN standards, in Belgium. Each standard produces data that allow relative ranking of the permeation parameters of pieces of gloves at the test conditions.

The characteristics of the main standards are presented, compared, and critiqued next.

ASTM F739—The ASTM F739 standard for continuous contact was issued in 1981[16] based on Nelson et al.[23] Revisions were made in 1985, 1991, 1996, 1999, and 2012.[16,24] Two polytetrafluoroethylene (PTFE) gaskets hold the glove material specimen vertically

between glass challenge and collection chambers (Figures 1 and 2).[16] The 2012 primary cell allows a material exposure/collection diameter of 2.54 cm (Figure 1) and the alternative cell material exposure diameter is 5.1 cm (Figure 2). Both have filling/sampling tubes and optional stopcock valves to facilitate different collection side configurations or continuous or static liquid challenges at 27 ± 1 °C. It might be noted that previous versions of ASTM F739 did not mention a standard temperature but did specify a user temperature variation of no greater than ± 1 °C. The 2012 standard does allow other temperatures to be used.

The 2012 standard defines the permeation test process in open-loop and closed-loop modes involving inert fluid (gaseous and liquid) collection media.[16] Air, nitrogen, and helium collection gases, and water collection liquid are recommended. If a collection medium interferes with the analytical method or degrades or back-permeates the glove, for example an organic collection solvent to collect a water-insoluble organic challenge chemical, an alternative has to be used. The open-loop system (Figure 3A) employing only fresh collection fluid allows calculation of permeation rate after accounting for collection fluid flow rate and glove collection side area relative to the measured concentration. There is no recirculation collection unlike the closed-loop system shown in Figure 3B that provides cumulated concentration permeated.[16]

The 2012 standard recommends that the collection medium flow rate be a minimum of 5 chamber volume changes per minute.[16] The flow rate in an ASTM open-loop permeation cell of 2.54 cm diameter and 20 cm^3 collection chamber volume should therefore be a minimum of 100 cm^3/min. The sampling/analytical method may be sequential or continuous but must detect a permeation rate of at least 0.1 μg/cm^2/min for both closed-loop and open-loop modes. The 2012 standard defined a closed-loop system as having a constant collection medium volume.

It may be difficult to detect the analyte in an open-loop system with gas collection medium if the permeant is not volatile (lower vapor pressure than 1 mm Hg at 25 °C or has a high boiling point beyond 150 °C at 1 atmosphere external pressure). Closed-loop collection may then become necessary. Nevertheless, the 2012 standard defined breakthrough times of different analytes irrespective of toxicity or volatility for both open-loop and closed-loop modes: breakthrough detection time (BT) and standardized breakthrough time (SBT), as well as SSPR, and cumulative permeation at a specified time (CP).

- BT is the time to detect the challenge chemical at the inner surface of the test material or in a collection medium. It is dependent on detector sensitivity.

- SBT is the time when a permeation rate of 0.1 μg/cm^2/min is reached within a minimum time window of 5 min. This parameter was called Normalized Breakthrough Time (NBT) before the 2012 standard but differed for the closed-loop method with a threshold value of 0.25 μg/cm^2.

- SSPR is the maximum constant rate of permeation. For an open-loop system with a direct reading instrument in-line, the measured concentration in the collection medium is directly proportional to permeation rate. When the measured concentration becomes constant, this signals the attainment of the steady state. The SSPR is then calculated by multiplying this constant

concentration in μg/liter by the collection medium flow rate in liter/min and then dividing the result by the glove piece area in cm^2 contacted by the collection medium. The 2012 standard also defines the SSPR in an open-loop system as when measured permeation rate values for samples at 5-min intervals have less than 5% relative standard deviation, with the average of four consecutive measurements being the SSPR. For a recirculating closed-loop system with direct reading instrument in-line, the linear portion of the cumulated mass (concentration) or cumulated mass/exposed area versus time curve defines the steady state period. The slope of the linear portion of a cumulated mass/exposed surface area versus time plot yields SSPR. Similarly, the slope of the mass vs. time plot provides the maximum mass transfer rate that produces SSPR when divided by the exposed surface area A.

- CP is the mass transferred by the end of the test permeation period, usually 2, 4, or 8 hr maximum for occupational exposures. The direct measurement of this parameter requires a closed-loop system. The CP can be calculated mathematically from open-loop mass transfer data.

Glove manufacturers use the open-loop with gas collection medium at room temperature for characterization of organic solvents via SSPR and BT, regardless of the toxicity and physical properties of the 167 and 18 standard chemicals/mixtures of the U.S. and the European Union, respectively. The capability of a collection gas system to capture all the permeated analyte affects method accuracy.[16,19] When not **all** the permeated compound is instantaneously evaporated from the collection side outer surface, this causes negative biases (longer BT and SBT, lower SSPR and lower cumulated permeation than true values), even for analytical methods with high sensitivities.[19] The problem may still be present in a closed-loop gaseous collection system. Schwope et al.[19] found no correlation in BT between the open-loop and closed-loop gaseous collection methods for the same compound.

Such a problem does not exist in a perfect closed-loop system using liquid collection with perfect instantaneous mixing, constant collection volume, with no contribution from penetration mechanisms, and no degradation/back-permeation by the liquid collection medium. In studies using volume replacement with solvent after sampling, accurate results may not occur when mixing or solubility are inadequate. In some closed-loop systems, the collection medium recirculates (Figure 3B).[16,21] The closed-loop liquid collection chamber without recirculation has one inlet to allow sampling/adding solvent (Figure 4).

The original ASTM cell (the alternative permeation cell of the 2012 standard) consisted of collection (100 ml volume) and challenge chamber diameters of 3.2 cm and 2.2 cm, respectively. The effective exposed and desorption surface diameter of material conditioned at room temperature is 5.1 cm. Pesce Lab developed the I-PTC-600 cell with 1-in. (2.54 cm) effective diameter of exposed material that produced equivalent permeation parameters but lowered hazardous waste disposal and chemical acquisition costs, and minimized volumes. [25] This configuration is now the primary 2012 ASTM standard permeation cell.

ASTM F739 does not specify the method of mixing in closed-loop systems without recirculation. Mechanical or magnetic stirring have been most used. The former is unwieldy

and the latter produces increasing temperatures during the permeation testing. To prevent concentration gradients in both the challenge and collection chambers and to control temperature, Mikatavage et al.[26] in 1984 developed a moving-tray thermostatted water bath technique. The ASTM permeation cells were submerged at 25 °C and the tray agitated at different velocities along the horizontal axis depending on the challenge type. The shaking force for 70 mL of challenge chemical and 58 ml of collection solvent without recirculation was optimized, to prevent concentration gradients, to achieve the same exposure and collection coverage areas, to simulate gentle hand flexing, and to maintain a constant area of contact by keeping the total collection side volume sampled to no more than 10%. Inadequate mixing occurred when the collection chamber was completely filled, even on shaking. The optimized air headspace volume caused turbulent mixing at the optimized tray agitation rate. For the I-PTC-600 2.54 cm ASTM type cell, the challenge/collection volumes were standardized at 10 cm^3 to accommodate emulsions, and the temperature ultimately set to 35 °C to mimic normal skin temperature.

ASTM D6978—Disposable medical gloves exposed to aqueous solutions of chemotherapy agents at their highest concentrations are evaluated over 4 hr at 30-min intervals according to ASTM D6978 published in 2005.[27] Here, the permeation cell is the large cell in ASTM F739 and is used under conditions of continuous contact in a closed-loop configuration without recirculation (Figure 4). The mixed collection liquid is either water or the aqueous solution in which the drug is dissolved, and sampling is done with replenishment of the collection liquid. The permeation temperature is 35 ± 2 °C (not 27 °C as for the ASTM F739 standard of 2012), and the breakthrough detection time (analogous to the standardized breakthrough time of the ASTM F739 standard of 2012) is set at 0.010 $\mu g/cm^2$/min rather than at 0.100 $\mu g/cm^2$/min. The thinnest portion of the glove from either the cuff or the palm is to be evaluated. The mandatory chemotherapy agents to be tested are: carmustine, cyclophosphamide, doxorubicin (adriamycin), etoposide, 5-fluorouracil, paclitaxel, and thiotepa. The minimum number of chemotherapy agents to be tested is nine. The standard was reapproved in 2013.

Non-ASTM standards—The initial ISO 6529 permeation cell of diameter 5.1 cm in 1990 used gravity with the analyte permeating downwards through the material clamped horizontally between the two cells, as had been standard in the Franz cell used in the pharmaceutical industry[28,29] and in skin permeation testing.[30] The next revisions, ISO 6529:2001 and ISO 6529:2013-2, adopted a cell similar to the contemporary ASTM F739 cell of diameter 5.1 cm and made the initial horizontal orientation cell alternative.[31] Other standards developed by the European Union, EN 374-3:1994, EN 374-3:2003, and EN 16523-1:2015 were also based on the ASTM 5.1 cm cell.[21] The EN and ISO standards allow the user to specify the permeation temperature. In November 2016, the EN and ISO standards were combined and denoted as EN ISO 374-1:2016. There was a minor update in 2018 denoted as EN ISO 374-1:2016/A1:2018.

The ISO 6529:2001, ISO 6529:2013-2, EN 374-3:2003, EN 16523-1:2015, and EN ISO 374-1:2016 emphasized five chamber volumes per minute as the minimum flow rate requirement for any permeation cell with a dynamic collection fluid (gas or liquid). EN ISO

374-1:2016 also requires that the degradation test EN 374-4:2013 and the penetration test EN 374-2:2014 were to be performed on the test gloves before permeation testing with EN 16523-1: 2015 that has now been replaced with EN 16523-1:2018. EN ISO 374-1:2016 also added six more chemicals (acetic acid 99%, ammonia 25%, formaldehyde 37%, hydrofluoric acid 40%, and hydrogen peroxide 30%, and nitric acid 65%) to be tested along with the previous chemicals (acetone, acetonitrile, carbon disulphide, dichloromethane, diethylamine, ethyl acetate, n-heptane, methanol, sodium hydroxide 40%, sulphuric acid 96%, tetrahydrofuran, and toluene). If breakthrough time at 1 μg/cm^2/min was 30 min for at least six chemicals of the list, this defined Category A gloves. Category B was defined if only three chemicals of the list met this breakthrough criterion. Category C was the classification when at least one chemical of the list had a breakthrough time of 10 min. The gloves in these categories were allowed to have the same standard pictogram (a conical flask containing liquid about to be grasped with a gloved hand) but with distinctive lettering denoting the categories "ISO 374-1:2016/Type X." The ISO version used a breakthrough time of 0.1 μg/cm^2/min.

Comparison of standards—The major standards are compared through time in Table 1.

Before 2012, the minimum collection side flow rate recommended by ASTM F739 was 50 cm^3/min for open-loop and recirculating closed-loop systems. All now agree on a minimum flow rate of five collection chamber volumes per minute for the permeation cell collection side for open-loop and recirculating closed-loop systems. The scientific evidence for the latter consensus follows:

Groce,[32] Chao et al,[21,33] IPCS,[18] Maekela et al,[22,34,35] and Mellstrom[36] compared permeation results of the then ASTM, EN, and ISO standards. The experimental studies at the same temperature now will be discussed.

Mellstrom[36] 1991 investigated toluene and 1,1,1-trichloroethane on three CPC neoprene (chloroprene) gloves using ASTM F739 and ISO 6529 standards, the latter with the material held horizontally. SSPRs were generally higher for the ASTM cell for 1,1,1-trichloroethane but lower for toluene.

Chao et al.[21] studied 1,2-dichloroethane and benzene against CPC nitrile and neoprene using ISO 6529 and ASTM F739 standards using the material held vertically in the open-loop system. Higher SSPRs were found for ISO cells. The SSPR data depended on collection gas flow rate. The recommended minimum flow rates were 75 and 150 ml/min for the ISO 6529 and ASTM F739 cells, respectively.

The permeation of 70% isopropyl alcohol through surgical disposable gloves using ASTM F739 and EN 374 methods indicated longer BTs in EN cells.[34]

Formaldehyde permeation from 37% formalin challenge was detected through natural rubber gloves, where the ASTM breakthrough times were 17–67 min, but the permeation rates were not high enough for breakthrough to have occurred according to the EN open-loop standards.[22]

All measured permeation rates for 4,4'-diphenylmethane diisocyanate challenges were below 0.1 μg/min/cm^2, and thus, the breakthrough times for all the eight tested glove materials were over 480 min, when the open-loop definitions of EN 374-3 and ASTM F 739 for the breakthrough time were used.[35] If instead the criterion of 1 μg/cm^2 was used, the chemical protective glove materials that had a breakthrough time of over 75 min were natural rubber, thick polyvinylchloride, neoprene-natural rubber, and thin and thick nitrile rubber. It was concluded that current ASTM F739 and EN 374-3 recommendations were not protective for a sensitizer like 4,4'-diphenylmethane diisocyanate.

Research gaps

The ISO and ASTM definitions of NBT or SBT of 0.10 μg/cm^2/min at about room temperature are not necessarily protective for all toxic chemicals, for example, like potent carcinogens, reproductive toxins, and chemical sensitizers. This situation may be better handled through a best available technology parameter like BT with analytical sensitivity of at least 0.010 μg/cm^2/min as for ASTM D6978-05 to define its detection time for chemotherapy drugs, most also being carcinogens. As mentioned previously, Maekela et al. also concluded that the existing open-loop breakthrough time criteria for a sensitizer like 4,4'-diphenylmethane diisocyanate[35] or for a carcinogen like formaldehyde[22] were inadequate to detect breakthrough, the gloves being labeled as "no breakthrough" actually permitting some but below the standard's breakthrough permeation rate.

A more realistic test temperature is another issue influencing actual worker risk, a factor recognized by ASTM D6978 for disposable glove testing at 35 °C. It is to be noted that ASTM F739 now sets 27 ± 1 °C as the standard permeation temperature (but still allows other temperatures) whereas previous versions of ASTM F739 let the user choose a permeation temperature but specified a temperature variation of no more than ±1 °C. At the very least, the permeation temperature of ASTM F739, EN 374, EN 16523, and ISO 6529 for disposable gloves should be 35 °C as for ASTM D6978. It would provide a margin of safety to mandate 35 °C for CPC since there are also thin and thick CPC materials, and CPC are worn for long times.

A research need in all the standards is how to detect reversible swelling or shrinking during permeation testing to add more evidence that Fick's first law truly is applicable for the permeation data generated. The current methodology detects irreversible swelling or shrinking but also does not have guidance on how much shrinking or swelling is cause for material rejection.

Another problem with the standards as written is the lack of scientific literature citation/evidence to justify the details of the procedures, for example, the basis for the choice of permeation standard temperature of 27 °C for the current ASTM F739 and of 35 °C for ASTM D6978. Another example is why the relative humidity (RH) of 30–80% and not a specific RH at 27 ± 2 °C was adjudged to be suitable for conditioning materials for 24 hr before and after permeation for the current ASTM F739.

Recommendations

The major permeation standards have become more harmonized, for example, with the material being vertical in the primary permeation cell and a minimum collection chamber flow rate of five collection chamber volumes. However, the standards are still not identical. It would be good for commerce and research if the standards were harmonized completely, adopting the same terms used and their definitions, permeation cells, and test conditions like temperature so as to minimize needless confusion, and to be more in line with conditions experienced by workers who are wearing gloves.

The 2.54 cm diameter permeation cell of ASTM F739 should be the primary permeation cell for all the standards including ASTM D6978.

A two-tier breakthrough time system that takes account of the toxicology of the challenge compound is also recommended: 0.010 $\mu g/cm^2/min$ at 35 °C for known/probable human carcinogens, reproductive and developmental toxins, and sensitizers; and 0.10 $\mu g/cm^2/min$ at 35 °C to define a normalized/standardized breakthrough time for other chemicals that are less toxic.

We also recommend the EN style of nomenclature as in EN 374: 2016 being used to denote future harmonized methods. The observant reader will note that this has been adopted throughout the text so far. ASTM denotes its 2012 F739 method as ASTM F739-12. ISO similarly has its 6529 method of 2016 as ISO 6529-2016. Since harmonization of EN and ISO is already occurring, harmonization will be faster if fewer countries have to change their statutes.

Whole glove permeation—The permeation standards discussed above are convenient because users can choose the permeation temperature and only a piece of the glove is needed for testing. In the workplace, a whole glove is donned, worn, and doffed, and experiences forces caused by handling work pieces.[37,38]

The scientific literature of whole glove permeation is described next, all studies being at room temperature unless specified otherwise.

Williams in 1981[39] measured breakthrough times at 3 $\mu g/cm^2/min$ and permeation rates of 1,4-dichloro-2-butene that was sprayed at a motionless whole glove (8 different glove types) on a stainless steel tubing artificial hand. An open loop nitrogen carrier gas collected the permeant from inside the glove. The breakthrough times and permeation rates were about the same as for glove pieces from and above the palm evaluated in a permeation cell with open-loop collection, nitrogen carrier, and with the test material held in the horizontal position but using the criterion of 0.1 $\mu g/cm^2/min$ for the breakthrough time.

Berardinelli et al.[40] in 1986 reported on the permeation of acetone through a whole neoprene latex glove. The glove was turned inside out, the acetone liquid added, the top of the glove tied off, and the hand clamped at the tie-off. A calibrated portable photoionization detector (PID) quantified the vapor from the permeated acetone from the outside. The thinnest parts of a glove which were between the fingers, back, and palm, had the shortest

breakthrough time and produced the largest steady-state concentration. The thickest part of the gloves, the fingertips, had the longest breakthrough time and the lowest steady-state concentrations.

Gunderson et al.[41] in 1989 showed that permeation of *m*-phenylenediamine in a amine hardener material through whole CPC nitrile gloves during onsite testing was indicated by its stain formation caused by its oxidation. Shorter BTs were found than in the laboratory. The stains appeared on an inner white cotton glove (sensitivity was at the microgram level) and were detected fastest at the points where the greatest hand pressure was exerted on the contaminated handle of a screwdriver used in the work activity.

A 1990 study of chemotherapeutic drugs through a surgical latex disposable whole glove at 37 °C featured a modified Franz permeation cell with a pneumatic flexion feature that produced no significant difference in NBTs but doubled the calculated diffusion coefficient for cyclophosphamide relative to no flexion.[42]

Perkins et al.[43] in 1997 reported the effects of hand glove flexure on acetone permeation using a CPC neoprene whole glove and on heptane permeation using a CPC PVC whole glove, with air inside the glove as the collection medium as part of an open-loop configuration. Glove weight at different times was measured. Although there was poor precision, there were significant increases for flexed relative to static situations for SSPR, and also significant decreases in BTs for both cases. For example, flexing decreased heptane's BT by nearly a factor of 2 and increased SSPR by 36–55%.

Boeniger and Klingner[37,38] in their 2002 reviews also advocated whole glove testing because the open loop ASTM F739 standard was not appropriate for over 80% of the chemicals with TLVs with a "skin" notation since their low vapor pressures (1 mm Hg at 25 °C) caused systematically long BT and low SSPR.

In summary, whole gloves experience forces during donning and doffing, and frequent flexion and extension after being donned. Further, there are glove temperature differences when hot and cold objects are handled, when hot and cold areas are entered, when gloves are tightly fitting or not, and when they are worn for different times.[37,38] Moreover, glove resistance and texture are affected not only by movement, flexion and extension, but also by other mechanical and physical motions such as pushing, pulling, lifting, and pressing objects as well as stretching hands while conducting individual or multiple tasks, all adding stress on the gloves that might result in hole formation and glove thinning at pressure points with enhanced permeation when co-exposed by solvent. In addition, cross-contamination when the gloves are donned and doffed can occur.

The nearest non-human system that could simulate whole glove permeation with the above points in mind is a dextrous anthropomorphic robot hand, one capable of moving the fingers and clenching the fist.

A dextrous robot hand whole glove system that used an inner cotton glove solid collection medium plus glove inner surface wiping was reported in 2008.[44] The system at 35 °C was used to assess the permeability of disposable nitrile gloves when exposed to an aqueous

emulsion of the pesticide captan at its highest recommended field spraying concentration.[44] No significant difference in CP at the end of 8 hr was observed between non-clenching and clenching hands. However, clenching caused some gloves to tear, and, as all permeation test methods measure the sum of penetration, degradation, and permeation, the tear resulted in a massive influx of challenge liquid into the cotton glove collection medium. The solid collection medium was potentially useful for solids and non-volatile liquids but was not amenable to continuous monitoring or intermittent sampling.

Mathews and Que Hee[45,46] studied the permeation of cyclohexanol through four different disposable nitrile gloves from Kimberly Clark Professional (KCP) using the same whole glove dextrous robot hand. Recirculating 35 °C water at 100 cm^3/min was the collection medium between the enclosing outer larger disposable nitrile glove and the inner CPC nitrile glove that protected the robot hand. The results were compared with the ASTM moving tray water bath technique developed by Mikatavage et al.[26] but using the 2.54 cm ASTM F739-type permeation cell at 35 °C. There were significant differences in NBT, SBT, and SSPR between the clenching (at 1.8 kg clenching force) and the non-clenching hand only for the thinnest glove, Sterling. The clenching hand had an average NBT/SBT that was about 0.5 times and an average SSPR was 1.61 times the values of the nonmoving hand tests. The ASTM moving tray water bath technique for the Sterling glove produced an average SBT 0.8 times and an average SSPR 1.17 times the values of the non-clenching hand tests. This also showed the gentle forces in the ASTM moving tray water bath technique caused enhanced permeation relative to an immobile whole glove. Glove thickness and porosity but not acrylonitrile content were the most important factors for enhanced permeation during clenching.[45]

Phalen and Wong[47] developed a whole glove permeation test based on a pneumatic system as a whole glove flexion device to evaluate the permeation of ethanol through 30 different types of disposable nitrile gloves. Air flow was used as the collection medium for the portable PID as an inline direct reading monitoring system. Pneumatic movement resulted in a shorter NBT and a higher SSPR than for the static hand in 28 and 25 of the gloves, respectively. One of the responsive gloves was Kimtech G5 Sterling which is not recommended for use with ethanol.

Banaee and Que Hee[48] repeated the Matthews study but with limonene for four types of KCP disposable nitrile gloves.[45,46] The SBT for the ASTM based method and the non-clenching hand for the Sterling glove was 15 ± 5 min. KCP, using an open-loop gas collection method at room temperature, reported a NBT for limonene of 105 min for this glove. There were no statistical differences at p   0.05 in SSPR for the clenching/non-clenching hand, and the ASTM moving tray water bath technique for the three thickest nitrile gloves (Blue, Purple, and Sterling). This was not so for the thinnest glove (Lavender) where the average SSPR for the clenching hand was 16% higher than for the non-clenching one, both also having SBTs of less than 10 min.

In summary, there is evidence to show that whole glove permeation standards would be useful for testing of the thinnest disposable gloves. However, the cyclohexanol and limonene ASTM moving tray data at 35 °C were not statistically different at p   0.05 from the

corresponding clenching/non-clenching dextrous robot hand data for the thicker disposable nitrile gloves, indicating adequacy of the ASTM moving tray method at 35 °C to predict permeation up to clenching forces of 1.8 kg. This also suggested that CPC nitrile gloves would not show differences for a clenching force of 1.8 kg. However, the thinnest glove in these studies did show differences on clenching, this being chemical dependent. The Phalen data did show decreases in NBT and increases for SSPR for hand movement when disposable nitrile gloves were challenged with ethanol. More research is needed to determine whole glove permeation with dextrous robot hands of greater clenching forces than 1.8 kg. More chemicals and disposable gloves need be tested to determine if the chemical-glove interaction varies with chemical and glove type on hand movement.

Conclusions

Some recommendations for the existing permeation standards include: harmonization of permeation cells, breakthrough time terminology and definitions including use of best available technology breakthrough time criteria for human carcinogens, potent reproductive toxins, and sensitizers; a standard permeation temperature of 35 °C as for ASTM D6978 for ASTM F739, EN 374, EN 16523, and ISO 6529 to provide a more realistic temperature that simulates a donned glove for a worker, and development of methods to assess reversible swelling or shrinking during permeation tests rather than just the current detection of irreversible swelling and shrinking.

The results for the whole glove model suggest that it would be most useful for the thinnest disposable gloves. These permeations depended on the chemical-glove material interaction that involved glove thickness uniformity, co-polymer content variation, porosity variation, and temperature as well as type of chemical. More research is needed to determine whole glove permeation with dextrous robot hands of greater clenching forces than hitherto used, and more permeation data needs to be generated for different chemicals under clenching and non-clenching conditions and with moving fingers.

Funding

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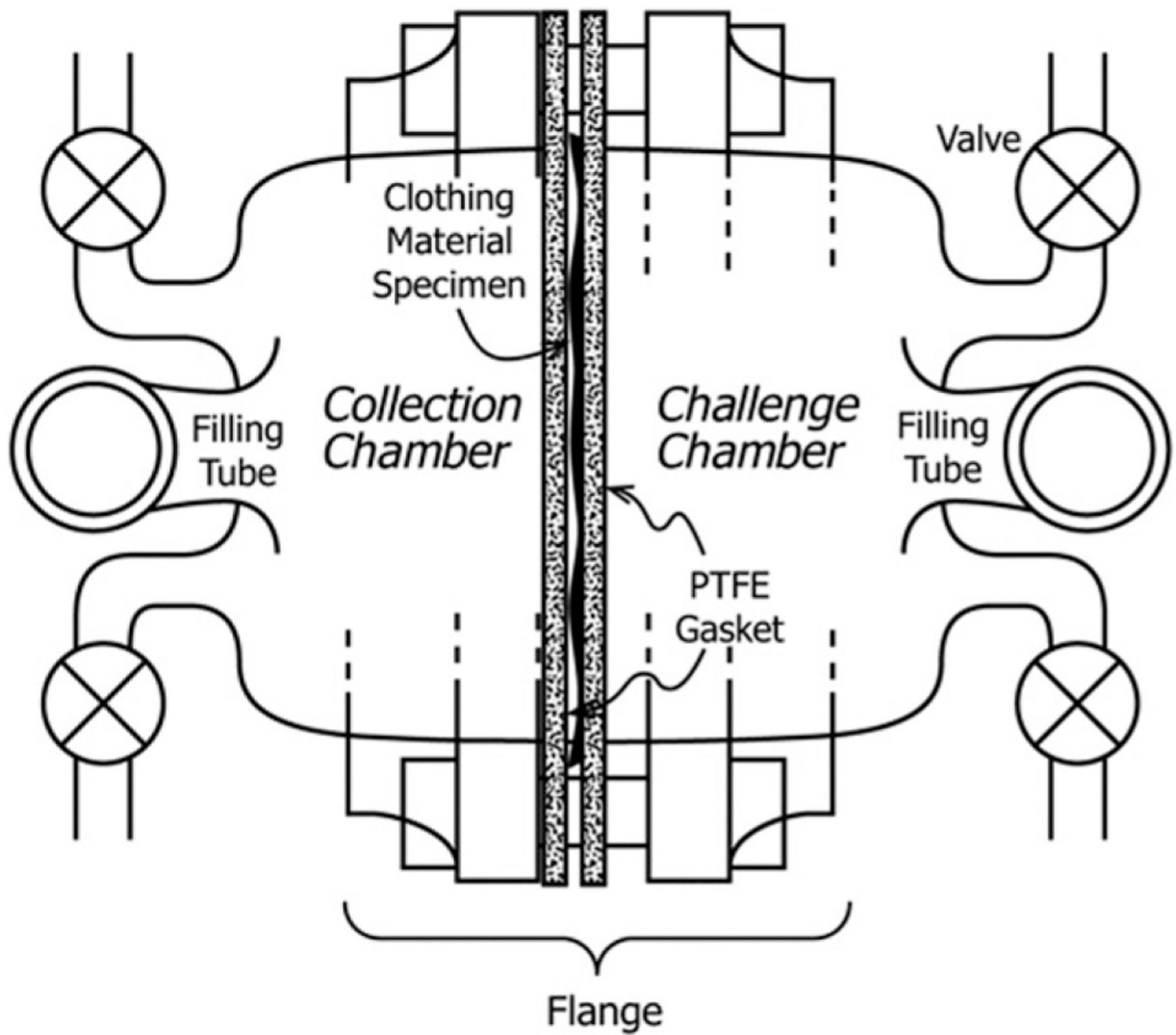
Figure 1.
ASTM F739-12 permeation test cell for liquid challenge chemicals, 2.54 cm in material area exposure diameter.[16] The permeant travels from the challenge chamber to the collection chamber.
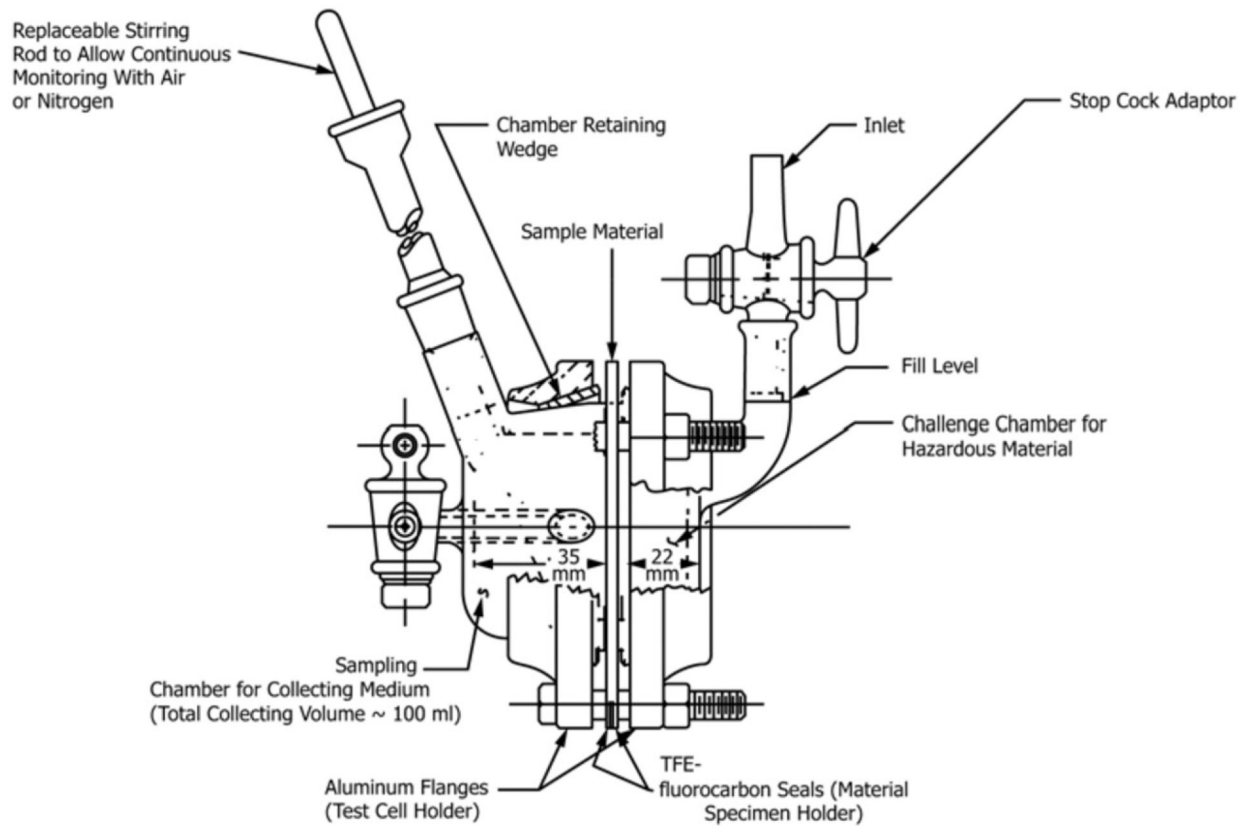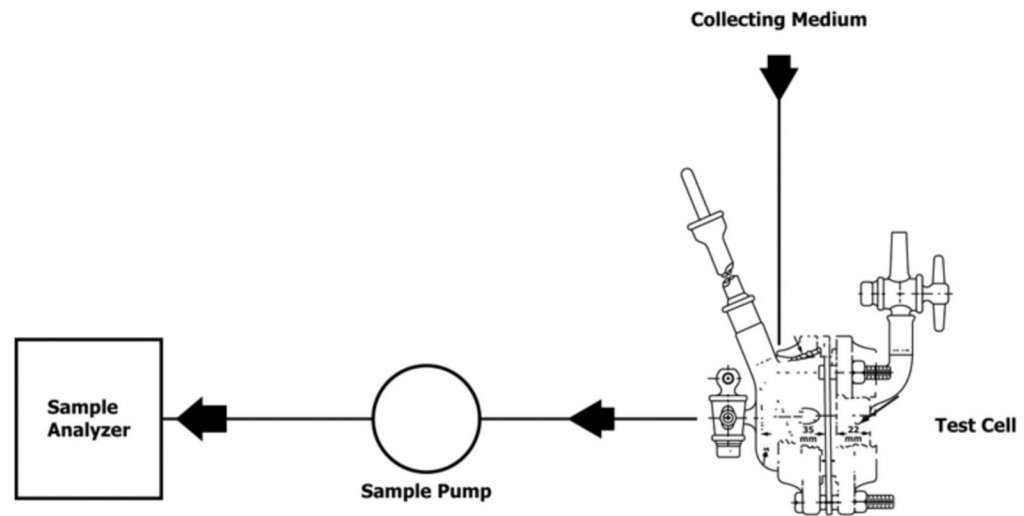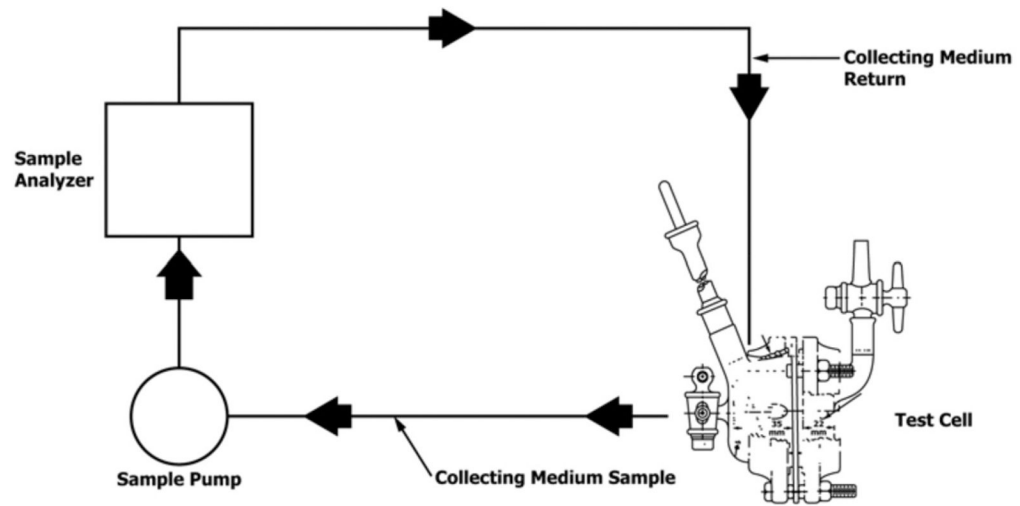
Replaceable Stirring Rod to Allow Continuous Monitoring With Air or Nitrogen

Chamber Retaining Wedge

Sample Material

Inlet

Stop Cock Adaptor

Fill Level

Challenge Chamber for Hazardous Material

35 mm

22 mm

Sampling Chamber for Collecting Medium (Total Collecting Volume ~ 100 ml)

Aluminum Flanges (Test Cell Holder)

TFE-fluorocarbon Seals (Material Specimen Holder)

Figure 2.
Alternative ASTM F739-12 permeation test cell.[16] The collection stirring rod directs gas collection medium towards the center of the material permeated. This was the original ASTM F739 cell.

Collecting Medium

Sample Analyzer ← **Sample Pump** ← **Test Cell**

A

Collecting Medium Return

Sample Analyzer

Sample Pump ← **Collecting Medium Sample** ← **Test Cell**

B

Figure 3.
ASTM F739-12 **A**: Open-loop permeation mode.[16] The sample pump may not be needed for a collection medium with sufficient positive pressure and if the sample analyzer has its own pump. **B**: Closed-loop system with recirculating collection medium.[16]
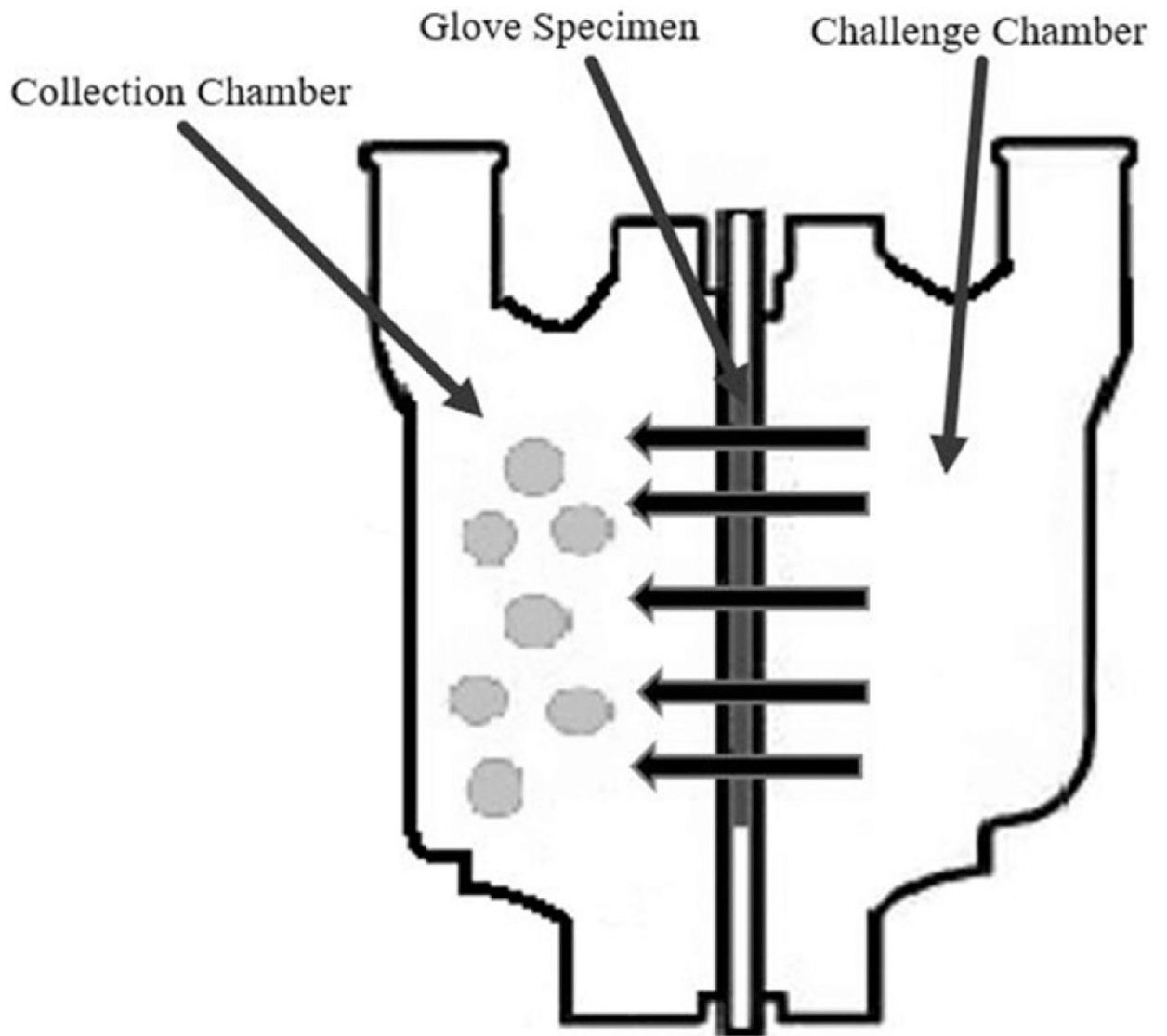
Figure 4.
Closed-loop permeation cell without recirculation collection. In practice, the collection side is either stirred or the whole cell shaken.

Table 1.

Determinant features in the ASTM F739, ISO 6529, and EN 374-3 Permeation Standards through time. No temperatures were specified except 27 ± 1 °C for ASTM F739 in 2012.

Standard Permeation Test Method (Year)	Cell Diameter[A]	Collection Medium Dynamic Flow (per min)	Minimum Permeation Rate[B] at NBT/SBT[C]	Outcome
EN 374–3 (1994, 2003, 2016)	5.1	Minimum 5 chamber volumes	1	NBT
ASTM F739 (1981,1985, 1991,1996, 1999)	2.5, 5.1	5 chamber volumes, Minimum 50 cm^3/min, Maximum 150 cm^3/min	0.1 (open) 0.25 (closed)[F]	NBT, SSPR
(2012)		Minimum 5[D] chamber volumes, 100 or 300 cm^3/min[E]	0.1 (open) 0.1 (closed)	SBT, SSPR
ISO 6529 (2001, 2013, 2016)	2.5, 5.1	Minimum 5 chamber volumes	0.1 or 1.0	NBT, SSPR

[A] Diameter in cm;

[B] Permeation rate in μg/cm^2/min;

[C] NBT/SBT, normalized breakthrough time/standardized breakthrough time;

[D] Five chamber volumes within first min of permeation;

[E] 100 cm^3/min for 2.5 cm cell, 300 cm^3/min for 5.1 cm cell;

[F] 0.25 μg/cm^2 for NBT (closed loop) before 2012.