World Health Organization

WHO Prequalification Programme / Vector Control Product Assessment

WHO Public Assessment Report: WHOPAR Part 3

SC Johnson Guardian

(S.C. Johnson & Son, Inc.)

P-12643

Quality Assessment

Contents

1 Chemical and physical data

1.1 Chemical and physical properties

SC Johnson Guardian is a vapor releasing product formed from a mesh substrate impregnated with transfluthrin welded in a plastic frame for use as spatial emanator.

Data on the chemical and physical properties of the active ingredient and the product SC Johnson Guardian were provided. These data were obtained from studies conducted according to established standards and/or Good Laboratory Practices (GLP) and are considered complete. Product specific properties are summarized in Table 1. Numerical results are presented as: mean (range). These summary results are based on the analysis of batches: 121420 L6T4, 1077D1, 1077D101, 1077D102, 1077D103, 1077D104.

Complete results from the studies 1077NA3, 1077NA1, 1077NA5, 1077A3, 1077A2, 1077A5, 1077A4, 1077A7are available in Appendix 1.

Table 1. Chemical and physical properties for SC Johnson Guardian

Data requirement	Test method ID	Result
Transfluthrin content	See Appendix 2	2.53 g (2.48-2.56 g) or (99.6-102.4% of the nominal quantity)
Treated surface area	See Appendix 2	333.17 cm^2 (331.05-334.89 cm^2)
Daily emanation rate (mean)	See Appendix 1 and 2	6.1 mg/day (5.4-6.9 mg/day)

No significant differences were recorded among the properties of the product kept at ambient temperature and after accelerated storage stability test conditions.

1.2 Manufacturing, composition and formulant information

Data on the manufacturing process and product composition for SC Johnson Guardian have been provided and are adequate. A summary is presented in Table 2. Detailed information on the manufacturing process and product formulation is considered Confidential Business Information (CBI).

Table 2. Manufacturing process and product composition data submitted for SC Johnson Guardian

Description of starting material	Transfluthrin TC formulated as part of the production process. The source of the active ingredient is supported by a current evaluation report confirming compliance of the materials with the established WHO specification.
Declaration of product formulation	Included in the confidential business information.
Production / formulation process	Transfluthrin technical active substance is dispensed onto a polyester (PET) mesh substrate. The mesh is welded in a PET thermoform frame. The product is packaged in multi-layer plastic flow-wrap. The individually wrapped units are packed into cartons of 108 units.
Discussion of impurities	No relevant impurities are present in the product.
Certification of limits	Transfluthrin: 2.5 g, acceptable limits 2.35-2.65 g

1.3 Enforcement analytical method

Table 3. Details of the analytical method used to determine transfluthrin in SC Johnson Guardian	
Quantification of transfluthrin	See Appendix 2

The method is appropriate for the determination of the active ingredient content of the product.

2 Overall quality conclusions

Based on the studies and information provided, all data requirements for the prequalification assessment of product quality have been satisfied. These data have been relied upon to assess the formulation, manufacturing process, and physical/chemical characteristics of the proposed product for the purpose of establishing the identity of the product and assuring that the product can be produced consistently.

The methods for assessing the physical/chemical properties of the product were validated methods.

The quality component of the dossier is considered complete, and the assessment of the submitted information on quality supports prequalification of the product.

Table 4. List of quality studies submitted to WHO as part of the prequalification dossier	
Studies that were relied upon for decision making	
Study number	**Study title**
1077A3	Storage Stability and Corrosion Characteristics of a Test Substance: Mesh After 36 Months at 20 °C
1077A4	Storage Stability and Corrosion Characteristics of a Test Substance: Mesh After 8 Weeks at 40 °C
1077A2	Storage Stability and Corrosion Characteristics of a Test Substance: Mesh After 8 Weeks at 40 °C
1077A5	Storage Stability of a Test Substance
1077A1	Validation of an Analytical Method: ARTM-SOF-72154
1077A7	Storage Stability of a Test Substance: Mesh After 2 Weeks at 54 °C
METHOD NO.: ARTM-SOF-72154	Quantification of Transfluthrin from a Mesh Spatial Repellent Using Gas Chromatography
1077NA6	Validation of an Analytical Method: SCJ-KE-TM-001
METHOD NO.: SCJ-KE-TM-001	SCJ-KE-TM-001-Determination of Transfluthrin in Guardian mesh finished Product (Code:374640)
1077NA5	Transfluthrin Determination During Spatial Repellent Emanation
1077NA1	Emanation of Guardian After 365 Days
1077NA7	Transfluthrin Content in SC Johnson Guardian
1077NA3	Treated Surface Area Determination of Guardian
1077NA2	Weight Loss Determination of Transfluthrin in Guardian

3 Manufacturing release specifications

3.1 Summary of manufacturing release specifications

Table 5. Summary of manufacturing release specifications for SC Johnson Guardian

Description
The vapor releasing product shall be formed from a polyester (PET) mesh substrate dosed with technical transfluthrin complying with the requirements of WHO specification 741/TC (current version). The mesh is welded in a PET thermoform frame and pouched within a multi-layer film. The product shall appear clean and shall be free from visible extraneous matter, visible damage (such as tearing of the film or mesh) and visible manufacturing defects (such as incomplete seal). The product shall be suitable for use as a spatial emanator.

ID	Property	Method	Declared value
1*	Sampling Plan	See Appendix 2	
2*	Transfluthrin content	See Appendix 2 (ARTM-SOF-72154)	2.5 g ±6%
3*	Treated Surface Area	See Appendix 2	339 ± 34 cm^2
4*	Mesh Conformity	See Appendix 2	The mesh is present, welded at all weld points (see Figures 5 and 6), and does not extend beyond the outer edge of the frame.

*Indicates that additional information is available in Appendix 2.

Manufacturers are expected to rely on the information above as part of a QC management plan and for validation of product quality when released. To the extent required, Certificates of Analysis to support the release of products should present results for the attributes identified in the above table.

3.2 Storage

Accelerated storage stability data were generated as per CIPAC MT 46.4 on SC Johnson Guardian. Test samples were stored for 8 weeks at 40 °C and 2 weeks at 54 °C. No significant differences were recorded among the properties of the product after accelerated storage stability test conditions.

36-month real time storage stability data at 20 °C (0,3,6,9,12,18,24,36 months' time points) were generated for SC Johnson Guardian. No significant differences were recorded among the properties of the product at time point 0 and after 36 months storage at 20 °C.

Products should be stored and transported in accordance with the conditions recommended by the manufacturer.

Where products have been subjected to prolonged storage, adverse conditions, or in opened/damaged packaging/containers, analysis and testing are recommended to assess changes in characteristics and their suitability for use.

Appendix 1. Summary of available data considered in Module 3

Batches used to generate the physical/chemical data

Batch number	Date	Uses
121420 L6T4	14/12/2020	emanation
1077D1	18/05/2021	5 batch analysis*, storage stability, semi-field
1077D101	06/03/2024	5 batch analysis*, storage stability**, semi-field
1077D102	01/04/2024	5 batch analysis*, storage stability**
1077D103	02/04/2024	5 batch analysis*
1077D104	04/04/2024	5 batch analysis*

* "5 batch analysis" refers to the analysis of all the properties in "Table 1. Chemical and physical properties for SC Johnson Guardian" for 5 batches. For batch "121420 L6T4" only the property emanation was provided.

Batches 1077D1, 1077D101, and 1077D102 were evaluated in 40 °C accelerated storage stability studies. Batches 1077D102, 1077D103, and 1077D104 were evaluated in a 54 °C accelerated storage stability study.
2-year ambient (real-time) storage stability data was provided for batch 1077D1.
** 2-year ambient (real-time) storage stability data using samples from batches 1077D101 and 1077D102 is in preparation for a future dossier update.

Product characteristics

Study 1077NA3 – Treated Surface Area Determination

Batch ID	Mean treated surface area (RSD)
1077D1	333.25 cm^2 (RSD 0.41%)
1077D101	332.15 cm^2 (RSD 0.55%)
1077D102	331.05 cm^2 (RSD 0.42%)
1077D103	334.52 cm^2 (RSD 0.30%)
1077D104	334.89 cm^2 (RSD 0.33%)

Appendix to Study 1077NA3 - Certificates of Analysis for each of the batches used in the study

Batch ID	Mean transfluthrin content (RSD)	As % of nominal
1077D1	2.49 g (RSD 0.8%)	99.6%
1077D101	2.54 g (RSD 0.8%)	101.6%
1077D102	2.56 g (RSD 0.4%)	102.4%
1077D103	2.55 g (RSD 0.4%)	102.0%
1077D104	2.54 g (RSD 0.4%)	101.6%

Batch ID	Mean AI content (RSD)		AI content range	
	Before storage	All results	Before storage	All results
1077D1	2.49 g (0.8%)		2.47-2.51 g	
1077D101	2.54 g (0.8%)	2.55 g (1.1%)	2.52-2.57 g	2.52-2.58 g
1077D102	2.56 g (0.3%)	2.55 g (0.6%)	2.56-2.57 g	2.53-2.57 g
1077D103	2.54 g (0.2%)	2.55 g (0.3%)	2.54-2.55 g	2.54-2.55 g
1077D104	2.54 g (0.3%)	2.55 g (0.4%)	2.54-2.55 g	2.53-2.56 g

Study 1077NA1 – Emanation of SC Johnson Guardian after 365 Days

Days	Weight of transfluthrin
0	2.48 g
28	2.33 g
63	2.15 g
91	2.00 g
119	1.86 g
147	1.73 g
182	1.57 g
210	1.44 g
240	1.29 g
273	1.13 g
301	1.01 g
329	0.91 g
365	0.78 g

The average emanation rate, calculated as (final weight of transfluthrin – initial weight of transfluthrin) / 365, was 4.7 mg/day for the mean of all three batches with a range of 3.92-5.45 mg/day for individual batches. Individual daily emanation rates are reported to range from 1.00 mg/day to 7.94 mg/day. The minimum effective period, calculated as the nominal amount of AI in the product divided by the highest reported individual emanation rate, is 314.86 days.

Study 1077NA5 – Transfluthrin Determination During Spatial Repellent Emanation

Batch ID	Mean daily rate	Minimum daily rate	Maximum daily rate
1077D1	5.4 mg/day	4.3 mg/day	8.3 mg/day
1077D101	5.8 mg/day	3.1 mg/day	9.4 mg/day
1077D102	6.7 mg/day	5.2 mg/day	8.2 mg/day
1077D103	6.9 mg/day	4.0 mg/day	8.9 mg/day
1077D104	5.6 mg/day	3.0 mg/day	8.5 mg/day
Combined	6.1 mg/day	3.0 mg/day	9.4 mg/day

Minimum and mean effective periods calculated from the target dose divided by the maximum and mean emanation rates respectively were 266.0 days and 409.8 days respectively.

Transfluthrin emanation rate and SC Johnson Guardian effective period

Average, minimum, and maximum emanation rates over the course of the study have been calculated by fitting a linear model to the relationship between Transfluthrin content (mg) and days emanating and analyzing the rate of change of the linear fit. The linear model can be represented by the equation below:

$$y = Ax + B$$

where: y= Transfluthrin content (mg)
x = time (days)
A and B are constant

Transfluthrin Content (mg) = Peak Area Ratio in Sample × Mean RF x 1000

where a factor of 1000 is used to convert the transfluthrin content determination to mg.

Area Ratio = Peak Area of Transfluthrin / Peak Area of DPP

$$\textbf{Response Factor (RF)} = \frac{\text{Transfluthrin Standard Weight (g)} \times \frac{\text{Purity (\%)}}{100}}{\text{Peak Area Ratio in Standard}}$$

The equations below were used to determine the effective period for the product.

$$\textbf{Minimum Effective Period} = \frac{\text{Target Dose Transfluthrin } (2500 \text{ mg})}{\text{Maximum Emanation Rate Observed } (\frac{\text{mg}}{\text{day}})}$$

$$\textbf{Mean Effective Period} = \frac{\text{Target Dose Transfluthrin } (2500 \text{ mg})}{\text{Mean Emanation Rate Observed } (\frac{\text{mg}}{\text{day}})}$$

Storage stability

Study 1077A7
Batch ID: 1077D102, 1077D103, 1077D104
Storage conditions: 2 weeks at 54 °C

Batch ID	Property	Before (Baseline)	After (54 °C)	Change
1077D102	Active Ingredient Content	2.53	2.48	-0.32
	Color	Frame: clear, colorless; Mesh: white with slightly yellow edges in some spots	Frame: clear, colorless; Mesh: white with slightly yellow edges in some spots	-
	Odor	Slight solvent	Slight solvent	-
	Physical State	Solid	Solid	-
	Corrosion	Not corrosive	Not corrosive	-
1077D103	Active Ingredient Content	2.53	2.48	-0.32
	Color	Frame: clear, colorless; Mesh: white	Frame: clear, colorless; Mesh: white with slight yellow edges in some spots	-
	Odor	Slight solvent	Slight solvent	-
	Physical State	Solid	Solid	-
	Corrosion	Not corrosive	Not corrosive	-
1077D104	Active Ingredient Content	2.53	2.48	-0.29
	Color	Frame: clear, colorless; Mesh: white	Frame: clear, colorless; Mesh: white	-
	Odor	Slight solvent	Slight solvent	-
	Physical State	Solid	Solid	-
	Corrosion	Not corrosive	Not corrosive	-

The reported AI content results were the means of duplicate determinations on three samples at each time point. The reported results for weight change were the means of three samples at each time point.

Study 1077A3
Batch ID: 1077D1
Storage conditions: 36 months at 20 °C

Month	AI content	Weight change	Frame	Mesh	Odour	Physical state	Corrosion
0	2.50 g	-	Clear, colourless	White with slight yellowing at edges	Odourless	Solid	Not corrosive
3	2.48 g	+0.03%	Clear, colourless	White with slight yellowing at edges	Odourless	Solid	Not corrosive
6	2.46 g	-0.01%	Clear, colourless	White with slight yellowing at edges	Odourless	Solid	Not corrosive
9	2.50 g	+0.02%	Clear, colourless	White with slight yellowing at edges	Odourless	Solid	Not corrosive
12	2.47 g	+0.08%	Clear	White with slight yellowing at edges	Odourless	Solid	Not corrosive
18	2.48 g	+0.04%	Clear	White	Odourless	Solid	Not corrosive
24	2.49 g	+0.08%	Clear, colourless	White with slight yellowing at edges	Odourless	Solid	Not corrosive
36	2.40 g	+0.06%	Clear	White with slightly yellow edges	Faint solvent-like, nutty	Solid	Not corrosive

The reported AI content results were the means of duplicate determinations on three samples at each time point. The reported results for weight change were the means of three samples at each time point.

Study 1077A2
Batch ID: 1077D1
Storage conditions: 8 weeks at 40 °C

Property	Before	After	Change
AI content	2.50 g	2.46 g	-0.04 g
Weight change	-	+0.03%	-
Frame	Clear, colourless	Clear, colourless	-
Mesh	White center with light yellowing on edges	White center with slight yellowing on edges	-
Odour	Odourless	Odourless	-
Physical state	Solid	Solid	-

The reported AI content results were the means of duplicate determinations on three samples at each time point. The reported results for weight change were the means of three samples at each time point.

Study 1077A5
Batch IDs: 1077D101 & 1077D102
Storage conditions: 9 months at 20 °C

Month	AI content	
	1077D101	1077D102
0	2.54 g	2.56 g
3	2.56 g	2.54 g
6	2.55 g	2.55 g
9	2.57 g	2.56 g

Study 1077A4
Batch IDs: 1077D101 & 1077D102
Storage conditions: 8 weeks at 40 °C

Property	Batch ID	Before	After	Change
AI content	1077D101	2.54 g	2.45 g	-0.09 g (-3.5%)
	1077D102	2.56 g	2.50 g	-0.06 g (-2.3%)
Frame	Both	Clear, colourless	Clear	-
Mesh	Both	White with slightly yellow edges	White with slightly yellow edges	-
Odour	Both	Odourless	Faint nutty odour	-
Physical state	Both	Solid	Solid	-
Corrosion	Both	No evidence of corrosion	No evidence of corrosion	-

Appendix 2. Manufacturing release specifications: Methods and notes

Description

- Dosed formulation may appear as a liquid, a crystallized solid, or a combination of both on the mesh substrate.

Sampling Plan

- Testing should be completed using the full product. Sub-samples should not be taken as representative of the whole product.

Attribute 2: Transfluthrin Content

Transfluthrin content will be declared as g/unit. The method ARTM-SOF-72154 was developed for Quantification of Transfluthrin from a Mesh Spatial Repellent Using Gas Chromatography. The method is appropriate for analyzing 2.5 g/unit (3.59 mg/mL) using dipentyl phthalate (DPP) for internal standard quantification.

A standard solution is prepared using transfluthrin with a known purity and DPP. Prepare a 5% w/v solution of DPP in acetone (i.e. ~12.5 g into 250 mL); this is the internal standard solution. Prepare a standard solution by weighing ~0.84 g transfluthrin into a 250-mL volumetric flask. Add 5 mL of DPP internal standard solution to the flask and dilute to volume with acetone, mixing well.

The sample is prepared by breaking down the sample frame to transfer the product into a glass jar and rinsing/extracting the transfluthrin with a known volume of acetone.

To prepare, fill a graduated cylinder with acetone to a known volume (recommended 100 mL), and remove the outer film of the product. Use heavy-duty stainless-steel scissors to cut slits in the plastic frame connected to the mesh. It is recommended to cut slits between the weld points on the frame so that the frame pieces stay attached to the mesh. Cut the frame over a glass dish/tray for collection in case pieces fall off. Using forceps, transfer the mesh and still attached frame pieces into a 1000-mL glass jar, folding the product gently to maneuver it through the opening. Push the product down to the bottom of the jar. Be careful not to contaminate the outside of the glass jar or hands while completing the transfer. Rinse the opening of the jar using the acetone from the graduated cylinder, and continue to rinse the forceps, baking dish, and stainless-steel scissors with the remaining acetone from the graduated cylinder. Pipette 15 mL of 5% DPP solution into the jar and add the remainder of 735 mL to the glass jar (i.e., if 100 mL was first used, add 635 mL; total solvent volume including internal standard solution is 750 mL). Ensure the product is contained under the solvent and close the jar.

Extract the product in a sonicating water bath for 1 hour. Once cooled, take an aliquot for gas chromatographic analysis. The following conditions allow for separation of transfluthrin and DPP over 9.375 minutes on a 30-m DB-1 (or equivalent) column using helium carrier gas and flame ionization detection:

Table 6. Gas Chromatographic Conditions for Analysis of SC Johnson Guardian

Column	Fused Silica Capillary Column, DB-1, 30 m x 0.32 mm ID x 0.25 µm
Injector Temperature	200 °C
Detector Temperature	300 °C
Carrier Gas Flow	25 to 50 cm/sec
Injector Split Flow Ratio	~45:1
FID Hydrogen Flow Rate	~ 30 ± 10 mL/min
FID Purified Air Flow Rate	~ 400 ± 20 mL/min
FID Make-up Gas Flow Rate	~ 30 ± 5 mL/min (He)
Injection Volume	1 µL
Oven Conditions	Initial temperature 175 °C Ramp 8 °C to 250 °C
Post-run Conditions	285-300 °C for 3 minutes

The area ratio of transfluthrin peak area to DPP peak area is used to quantify the transfluthrin content (g) per sample, using the peak area ratio of the standard solution with known transfluthrin content and a concentration factor of 3, accounting for the different sample and standard solution volumes. The calculations are as follows:

$$\text{Area Ratio} = \text{Peak Area of Transfluthrin} / \text{Peak Area of DPP}$$

$$\text{Response Factor (RF)} = \frac{\text{Transfluthrin Standard Weight} \times \frac{\text{Purity (\%)}}{100} \times \text{Concentration Factor}}{\text{Peak Area Ratio in Standard}}$$

$$\text{Transfluthrin Content (g)} = \text{Peak Area Ratio in Sample} \times \text{Mean RF}$$

Where Concentration Factor = 3.

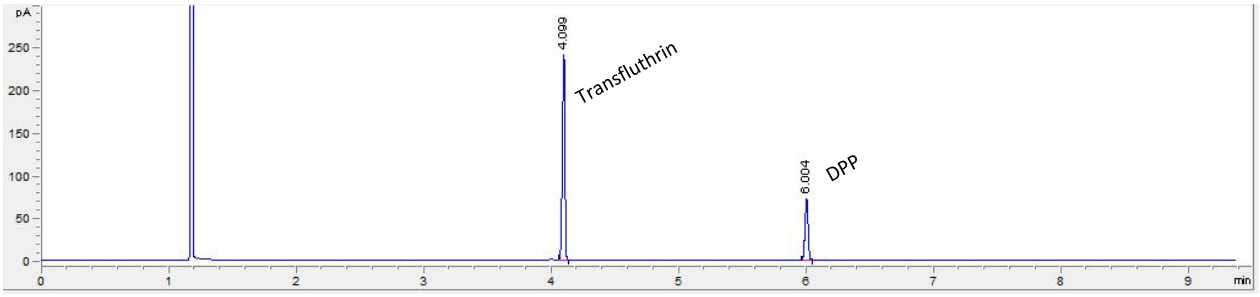

Figure 1. Representative chromatogram, transfluthrin and DPP standard solution

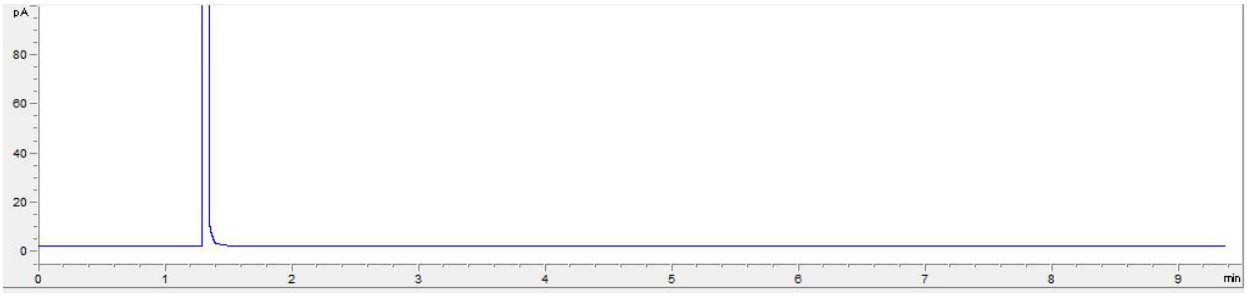

Figure 2. Representative chromatogram, un-dosed mesh product

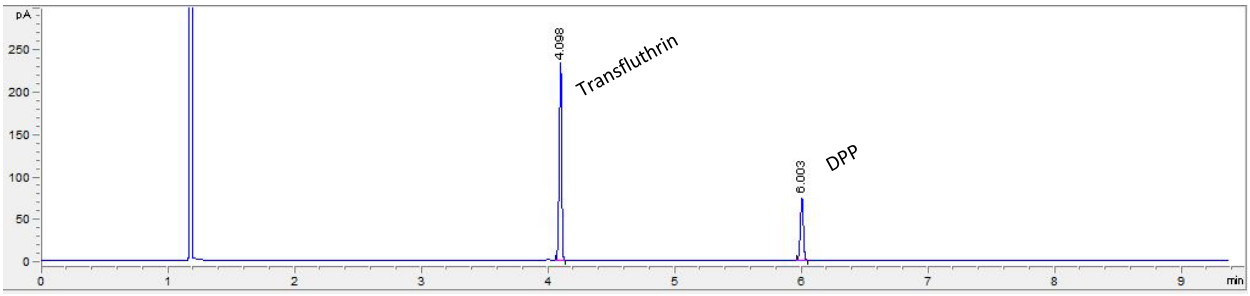

Figure 3. Representative chromatogram, SC Johnson Guardian

Attribute 3: Treated Surface Area

The treated surface area of SC Johnson Guardian can be determined by measuring the length and width of the mesh substrate as denoted in Figure 4. Measurements should be taken from one edge of the substrate to another, including any part of the mesh substrate under the frame, using a calibrated measurement tool, such as a ruler or caliper. Avoid taking measurements across frame weld points.

The following equations can be used to determine the total treated surface area of the product.

Equation 1: Mean Length = $\frac{(Length\ 1 + Length\ 2)}{2}$

Equation 2: Mean Width = $\frac{(Width\ 1+Width\ 2)}{2}$

Equation 3: Total Unit Treated Surface Area = Mean Length x Mean Width

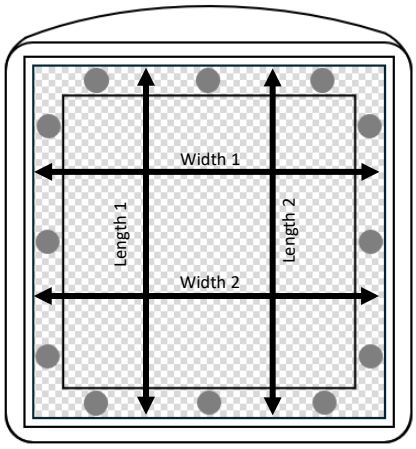

Figure 4. Diagram of SC Johnson Guardian for Treated Surface Area Measurements (for reference only, not drawn to scale)

Attribute 4: Mesh Conformity

Mesh conformity of the product is used to affirm the treated surface area. To confirm the product quality, a visual check can be performed on the product to ensure that the mesh is present, welded at all weld points (as outlined in Figure 6), and does not extend beyond the outer edge of the frame. See Figure 5 and Figure 6 below for a visual representation of passing mesh conformity.

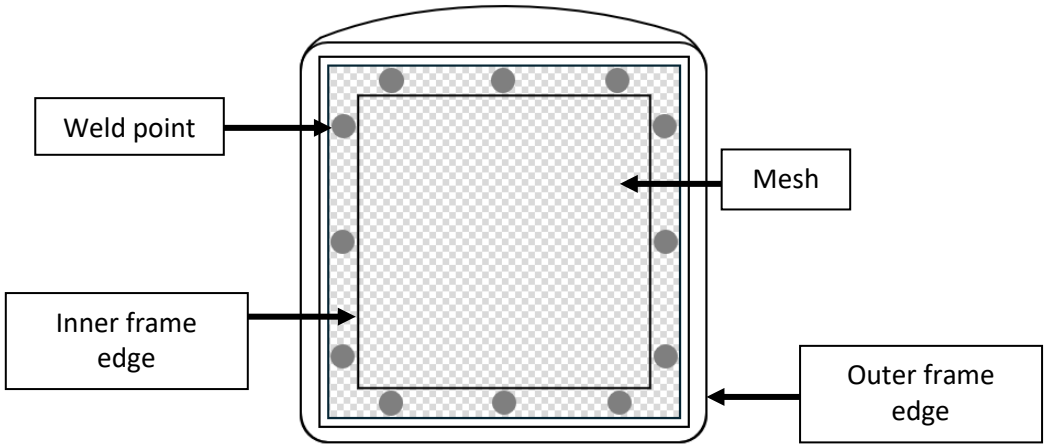

Figure 5. Diagram of SC Johnson Guardian for Visual Inspection of Mesh Conformity (for reference only, not drawn to scale)

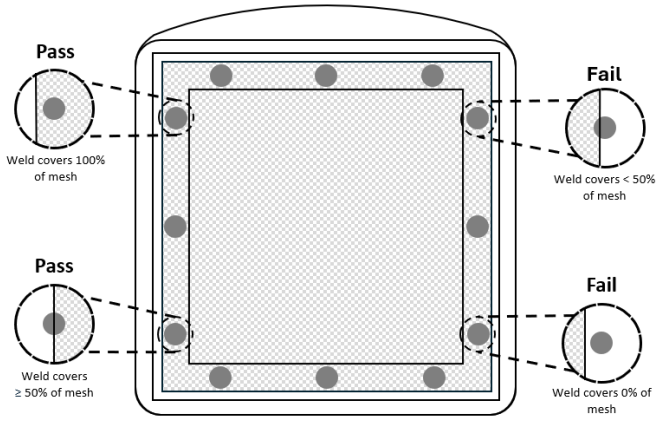

Figure 6. Diagram of SC Johnson Guardian Defining Visual Pass/Fail Criteria of Weld Coverage to Determine Mesh Conformity (for reference only, not drawn to scale)