Nipro Glass

STRONG PRESENCE IN THE GLASS PACKAGING INDUSTRY

This articles gives us an overview of one of the world's largest glass manufacturers – Nipro Glass. Since its founding more than 60 years ago, this globally-based company has continued to develop, becoming a major supplier to the top 10 pharmaceutical and biotech brands, and has 14,568 employees worldwide.

THE BEGINNING

In July 1954, Nippon Glass Shoji Co. was established in Shimogyo-Ku of Kyoto city and initiated sales of glass tubes for use in the production of ampoules and pharmaceutical vials. Almost 60 years after its establishment, Nipro embarked on a journey to become a major world class, glass producer/supplier, setting out to make a strong presence in the glass packaging industry. In 2011, Nipro acquired Amcor Glass, with factories located in France, Belgium and the United States of America, now respectively Nipro Glass France, Nipro Glass Belgium and Nipro Glass Americas. Further expansion continued with a greenfield Converting operation in Russia and a re-organized Tube Drawing facility in India. In 2012, Nipro acquired MGlass AG and MG Sterile Products AG, now Nipro Glass Germany and Nipro Sterile Glass Germany.

Key facts

Nipro Glass is currently the third largest glass manufacturer worldwide with 19 manufacturing sites located in the United States, France, Belgium, Germany, Russia, India, Indonesia, China and Japan. Nipro Glass is a major supplier to the top 10 Pharmaceutical and Biotech brands, and has 14,568 employees worldwide.

In each business area, Nipro Corporation focuses on building long-term partnerships with each and every customer.

COMPANY GOAL: ZERO-DEFECT QUALITY LEVELS

To facilitate optimal efficiency and maintain product integrity, Nipro's glass products are designed and manufactured to the highest quality standards. The company is a vertically integrated global supplier of pharmaceutical grade glass tube packaging.

Nipro's neutral clear NSV51 glass tube is fused and drawn in both its Aumale, France plant and its Millville, New Jersey, US plant. The company's W33 glass tube is produced in Millville, with high chemical durability and resistance to thermal shock. Nipro Glass utilizes both the Danner and the Vello continuous processes for drawing glass tubes. Both glass types meet Type I Borosilicate Glass standards, as specified by the current United States, European and Japanese Pharmacopeia (USP, EP and JP), as well as the American Society for Testing and Materials (ASTM).

Continuous improvement

The Nipro Quality Management System began with establishing a quality mindset. The company's management team and employees are committed to quality and Nipro provides its employees with continuous training through progressive education. Within the Nipro Group, Continuous Improvement aims at maximizing opportunities and making optimal use of existing resources to enhance the company's efficiency and competitiveness.

The company's in-line camera inspection system not only results in superior products, but also provides means to capture and quantify internal capabilities, enabling continuous improvements in processes.

At both Aumale and Millville factories, Continuous Improvement is a priority within each department, enabling to continuously address market needs, generating sustainable value for customers.

Millville and Aumale sites work with shared systems to ensure consistency in product, processes, and technology across Tube Draw operations. This also allows for multi-site sourcing and adds flexibility and contingency planning to meet the market's needs.

Best practice sharing is utilized across sites and both Millville and Aumale sites are ISO certified: ISO 9001:2008; ISO 14001:2004; OHSAS 18001:2007.

Monitoring and tracing

Quality control spans all processes, from the batch house, where raw materials are received and mixed, through the melting and forming processes, to tube finishing, packing and warehouse storing.

Manufacturing lines in Aumale and Millville are equipped with in-line automated vision inspection systems that inspect every glass tube. Moreover, manual inspection comes as a back-up, in order to ensure that all quality parameters are met, both dimensional and cosmetic.

Statistical Process Control (SPC) methodology provides control of Nipro's process at the point of manufacturing. The SPC systems in Aumale and Millville allow shop floor employees to make real-time, data driven decisions to the process, thereby reducing variability and scrap.

Technical characteristics

The following technical characteristics apply to Type 1 borosilicate glass tubes, in particular W33, NSV51 and NSV51 with cerium, glass types manufactured in Millville and Aumale.

Borosilicate glass, with its high hydrolytic resistance, is particularly suitable for the manufacture of primary containers or pharmaceutical use. Nipro Glass certifies that the Borosilicate glass we produce meets the requirements for Type I glass as set forth in applicable sections of the US and European Pharmacopeia and will also meet the requirements for arsenic extraction.

Nipro Glass further certifies that the glass meets the requirements in the Japanese Pharmacopeia for Glass Containers for Injections, as well as the ASTM 438-90 Specification for Laboratory Glass.

Sampling criteria

The lower limit of acceptability of a defect is defined by the AQL attributable to this defect according to the ISO 2859-1 and/or Mil Std 105E (ANSI Z1.4) standards. The AQL is defined as the level of quality, which, over a continuous series of batches selected for the purposes of inspection by sampling, can be considered as the limit for a satisfactory process, on average.

The frequency and population of each sample destined for inspection during production, for each characteristic, are defined hereafter.

Unless otherwise agreed upon between Nipro Glass Quality Management and our customer, production runs of glass tubing shall be sampled in accordance with ANSI Z1.4, Single, Normal, Level I. Customers' 'lots' or units for inspection are given quantities of glass tubes delivered as one shipment. This shipment may be all or part of a purchase order or production run, but the unit for inspection shall not have mixed production lots.

Other sampling levels or lot definitions may be employed by the customer for their own purposes and inspection economics; however, Nipro Glass recognizes the above plan as criteria for rejection or acceptance which is consistent with this industry.

INSPECTION METHODOLOGY

All glass tubes may have one or more imperfections, however not all imperfections constitute a

TABLE 1

DIMENSIONAL QUALITY

Characteristic	Defect description	AQL
Outside diameter	When the 2-point is not met over a continuous section of 60mm on the tube length	0,25
Inside diameter	When the 2-point is not met in the calculated measurement	0,25
Wall weight/Thickness	When the average of the minimum and maximum wall thickness does not meet the tolerance	
	>0.5% of the nominal outside diameter <20mm tube	0,25
Out of round/Ovality	>0.7% of the nominal outside diameter 20-30mm tube	
	>0.8% of the nominal outside diameter <30mm tube	0,25
Siding	>6% of nominal thickness	0,25
Length	NSV51 glass ±2mm of length specified by client	
	W33 glass ±1/4" (±6.35mm) of length specified by client	0,25
Bow	>0.8mm at 1m distance apart	0,25
Taper	In general, the value must not exceed 50% of the tolerance range for the outside diameter.	
	As requested by client	

Exceptions: Variations due to the presence of defects in the glass (stones/knots/ glassy inclusions) are not considered as defects.

non-conformity. Inspection covers three basic areas for conformity to specification: Dimensional, Functional and Visual.

Dimensional

Non-conformities refer to deviations outside of specifications. Applicable physical characteristics will be verified with appropriate gauges, tests and measuring techniques as applicable. Nipro Glass will provide the default measurement method and criteria unless other agreements are made.

Functional

Characteristics include certain tests for glass types such as those listed in the U.S. Pharmacopoeia (USP), European Pharmacopoeia (EP), Japanese Pharmacopoeia (JP) and ASTM standards as defined in our Certificate of Compliance.

Visual

Characteristics include flaws and imperfections inherent with glass tubing manufacturing termed 'visuals'. Colour variations and secondary operations are included as separate criteria and do not adversely affect fit or function of the finished product, unless specifically defined and agreed upon between Nipro Glass and the customer. Many visual conditions are not necessarily non-conformities and are subject to human judgment. Appropriate limit samples are established, where required, to assist in that judgment. Limit samples are defined as the maximum conditions allowable for acceptance. In the absence of agreed upon limit samples, Nipro Glass will default to the Nipro Glass internal limits established. All visual inspection is to be conducted with the unaided eye (zero per cent magnification), at a distance of 14-18 inches and under fluorescent lighting conditions with no black/white background, unless otherwise agreed upon.

Outside Diameter

The on-line diameter system measures the external diameter in a plane throughout the entire length of the tube and rejects all tubes that fall outside the limits.

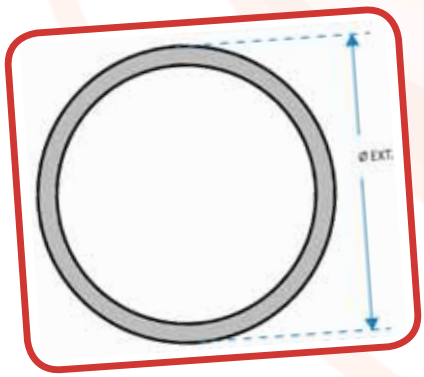
The outside diameter is measured using a digital micrometer between two parallel points on the outer surface of the tube.

Inside Diameter

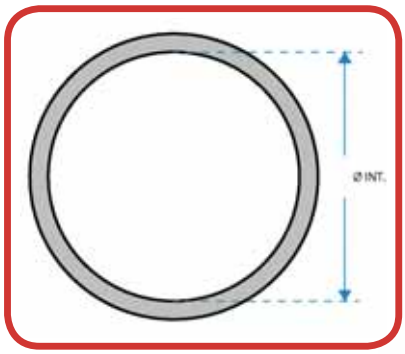
Difference between the tube's external diameter and its wall weight. The inside diameter is a calculated measurement of the difference between the measured outside diameter and the measured wall weight.

Wall Thickness/Wall Weight

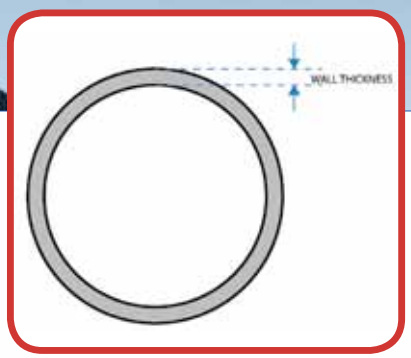
Nominal thickness of the glass



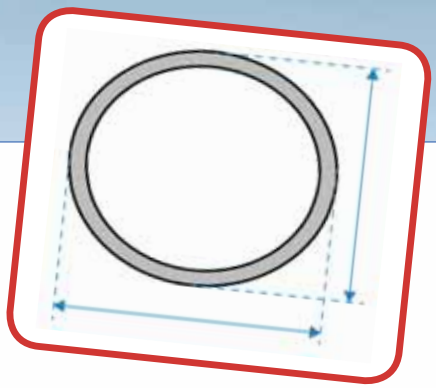
Outside Diameter



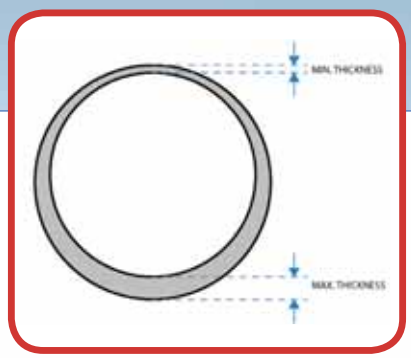
Inside Diameter



Wall Thickness/Wall Weight



Out of Round/Ovality



Siding

between the inner and outer surface of the tube. Regular measurements of the thickness are made using a digital gauge.

Two-point average of minimum and maximum measurement must average with the specification.

Out of Round/Ovality

Difference between the minimum and maximum outside diameters across a section of the tube. Regular measurements of out of round are made with a specific instrument measuring the diameters. The minimum and maximum outside diameters are measured.

Out of Round/Ovality is calculated by taking the difference between the minimum and maximum outside diameter in a cross section of the tube.

Tolerances are based on the diameter dimension. On a radius base calculation, the tolerance values would be half of those based on the diameter control measurement.

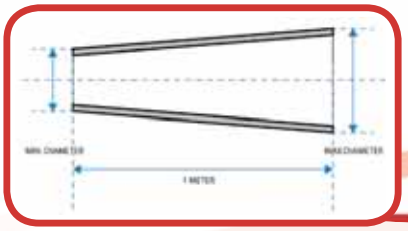
Siding

Difference between the minimum and maximum thicknesses in a given tube cross-section. Identify the minimum and maximum points on the circumference of the sample.

Taper

Difference between the minimum and maximum outside diameters along the same tube in 1 meter length. Specific checks only on customer request.

Taper = diameter max – diameter min



Taper

Length

Length

Distance between two planes vertical to the tubing axis at the ends of a tube.

Note:

- Standard Length for NSV51 Glass is 1500 millimetres ± 1 millimetres
- Standard Length for W33 Glass is 60” ± 1/4”

Bow

This represents the longitudinal curvature of the tube. Curvature is measured between two points which are 1m apart and must not exceed 0.8 millimetres. Bow is equal to one-half the total radial run-out in 1 meter of tube length.

The tubes are cut to specific lengths and each end is fused to a certain degree. The main types of end finishes are:

Very light, no tube deformation
Slight bulb edge
Slight re-entrant bulb edge
Significant bulb edge, clearly re-entrant. The residual internal

TABLE 2

END FINISHES OFFERED

The tubes are cut to specific lengths and each end is fused to a certain degree. The main types of end finishes are:

	Definition
Type N	Very light, no tube deformation
Type S	Slight bulb edge
Type M	Slight re-entrant bulb edge
Type H	Significant bulb edge, clearly re-entrant. The residual internal diameter will average between 45% and 70% of the nominal external diameter.
Type C*	Closed over end finishes with a small hole on one end of the tube only

*Not applicable for all tubing sizes

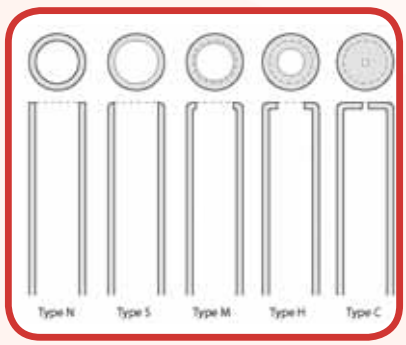
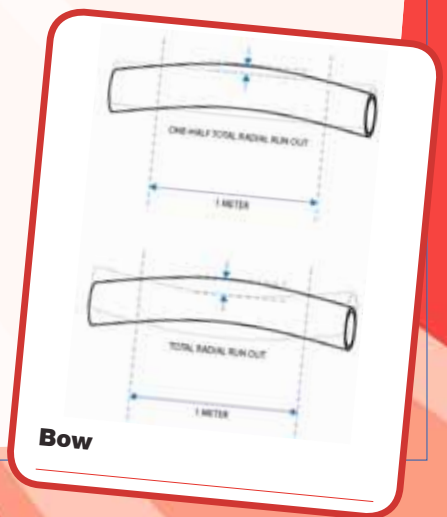


Diagram representing the measurement



Bow

Airlines

diameter will average between 45 and 70 per cent of the nominal external diameter. Closed over end finishes with small hole on one end of the tube only * Not applicable for all tubing sizes W33 glass is available in Type M and Type H End Finishes

Airlines

Airlines are bubbles of gas created during the melting operation that are elongated by the process of forming the tube. Airlines that exceed 15 millimetres in length and 0.03 millimetres in width are considered to be defects.

Any area where more than one airline appears, for cumulative airline purposes, the length of the area is only counted once. Quality level (AQL) measured in percent length in sample size.

Tolerances - The sum of the length of the defective airlines must exceed five per cent of the cumulative length of the sample size. Sample size to be ten random full lengths of tube.

Seed

An elongated gaseous inclusion (bubble) longer than five millimetres, and shorter than 15 millimetres, equal to or wider than 0.03 millimetres in width. May also be known as a short airline.

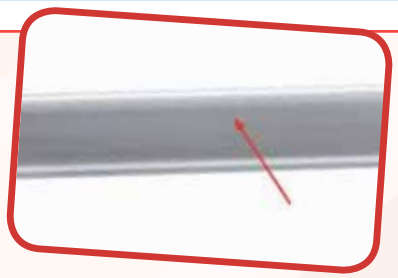
Stones/Knots

Stones occur as a result of undissolved batch or crystallized refractory material or glass components appearing in the form of an opaque inclusion in the wall of the tubing.

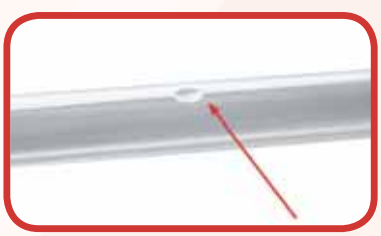
TABLE 3

VISUAL QUALITY

Characteristic	Default description			AOL
Intermixture	Intermixtures within a batch or unit are not allowed			None allowed
Check	No reference to size. The total length of the tube is considered, except for the first 3 cm from each end.			0,025
Crack	No reference to size. The total length of the tube is considered, except for the first 3 cm from each end.			0.025
End crack	No reference to size.			0.65
Scratches	For a non-surface treated tube: the cumulative length of scratches must not exceed 4% of the cumulative length of the sample size. For a surface-treated tube: the cumulative length of scratches must not exceed 3% of the cumulative length of the sample size. Sample size to be ten random full lengths of the tube.			AQL by percent (%) in sample
Airline	The sum of the length of the default airlines must not exceed 5% of the cumulative length of the sample size. Sample size to be ten random full lengths of the tube.			AQL by percent (%) in sample
Seed	More than or equal to 10 seeds per tube to be counted as one default. Sample size to be ten random full lengths of the tube.			AQL by count in sample.
Stones/Knots	≥0.5mm and ≤0.8mm			2.50
	Core > 0.8mm			0.10
Surface Impurity Easily removable not considered a defect	Exception to easily removable:			
	Glass pa rticles ≥ 0.5mm			0.10
	Internal/External: Not easily removable and ≥ 1.5mm			0.25
Particles (Inside Tube) *in particle count	Tube Diameter (mm)	*Particles > 0.2 and < 0.5mm	*Particles > 0.5mm	
	< 15.00	NMT 5	NMT 1	0.65
	≥ 15.00 to < 25.00	NMT 7	NMT 2	1.50
	≥ 25	NMT 10	NMT 2	2.50



Seed



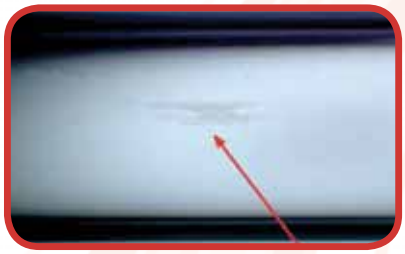
Stones/Knots

Tolerances

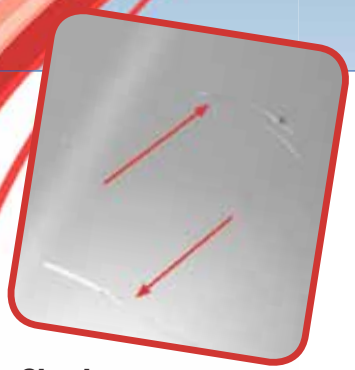
Stones/knots with a core of ≥ 0.5 millimetres and ≤ 0.8 millimetres
AQL 2.5
Stones/knots with a core of > 0.8 millimetres
AQL 0.1

Surface Impurities

Surface impurities are organic and inorganic substances that are neither contained in the glass composition nor are they eas-



Surface Impurities



Checks

Cracks

ily removable. Surface impurities are visible to the unaided eye under fluorescent lighting conditions. * Easily removable surface impurities are not considered as a defect.

Exception to easily removable
- Glass particles ≥ 0.5 millimetres
AQL 0.1
Internal/ External
Not easily removable and ≥ 1.5 millimetres
AQL 0.1

Checks

A check is a fracture that penetrates the surface of the tube. A check may significantly reduce the mechanical strength of a tube and interfere with thermal processing of the tubing. The total length of the tube is considered, except for the first three centimetres from each end.

AQL 0.025

Cracks

A crack is a fracture that runs deep into - or completely penetrates - the glass wall of the tube. A crack may reduce the mechanical strength of a tube and interfere with thermal processing of the tubing. The total length of the tube is considered, except for the first three centimetres from each end.

AQL 0.025

End Cracks

End cracks are fractures that propagate from the end of the tube and can significantly reduce the mechanical strength of the tube.

AQL 0.65

Scratches

Surface wear that can occur during the manufacturing process, transport, handling or use. Quality level (AQL) measured in percent length in sample size

Tolerances
- Scratches in the first five centimetres at each end are ignored.
- For a non-surface treated tube:
The cumulative length of scratches must not exceed four per cent of the cumulative length of the sample size. Sample size to be ten random full lengths of tube.
- For a surface treated tube:
The cumulative length of scratches must not exceed three per cent of the cumulative length of the sample size. Sample size to be ten random full lengths of tube.

Particles (inside tube) - Defined as particles of glass.
Tolerances - Quality level measured in particle count
- Tube Diameter < 15.00 millimetres
- Particles > 0.2 and < 0.5 millimetres 5
- Particles > 0.5millimetres 1 AQL 0.65
- Tube Diameter ≥ 15.00 to < 25.00millimetres
- Particles > 0.2 and < 0.5millimetres 7
- Particles > 0.5millimetres 2 AQL 1.50
- Tube Diameter ≥ 25.00 millimetres
- Particles > 0.2 and < 0.5 millimetres 10
- Particles > 0.5 millimetres 2 AQL 2.50

Intermixture

Intermixture implies the presence of any other product in a deliverable unit.

Examples
- Type of glass
- Varying dimensions
- Incorrect labelling

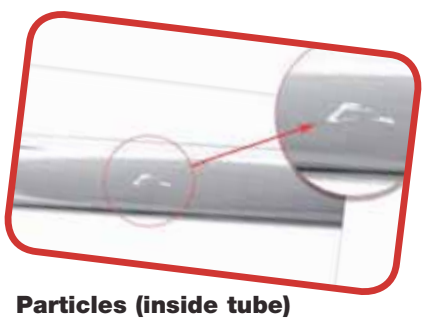
Intermixtures within a batch or unit are not tolerated

AQL none allowed

Labels

In general, each bundle (where applicable) and each pallet have a single discrete label. Faulty or illegible text on the labels is not permissible. Lot numbers/control numbers are assigned to each manufacturing lot and/or pallet, providing traceability to the date and period of time of manufac-

Scratches



Particles (inside tube)

TABLE 4

TOLERANCE STANDARDS - SYRINGE AND DENTAL CARTRIDGES (NSV 51) - SYRINGE TUBING

Outer diameter	Inner diameter	OD Tolerance (mm)	ID Tolerance (mm)
6.85	4.65	0.10	0.10
8.15	6.35	0.10	0.10
10.85	8.65	0.10	0.10
14.45	11.85	0.10	0.10
17.05	14.25	0.17	0.15
22.05	19.05	0.17	0.15

TABLE 5

TOLERANCE STANDARDS - DENTAL CARTRIDGE TUBING

Outer diameter	Inner diameter	OD Tolerance (mm)	ID Tolerance (mm)
8.65	6.85	0.10	0.10
10.85	8.65	0.10	0.10
10.95	9.25	0.10	0.10
11.60	9.70	0.10	0.10
14.00	12.00	0.11	0.10
14.45	11.85	0.11	0.10
18.25	16.05	0.13	0.13

turing. Labels will identify the product with the following minimal information:

- Lot number/Control number
- Pallet Number
- Date of Production
- Production Site
- Glass Type
- Outer Diameter, Wall thickness and Length

Additional information may be provided at customer request.

Chemical resistance

Many tests have been developed to measure glass durability and the hydrolytic resistance of glass, as glass extractables and leachables may cause a pH shift in the aqueous solution. The hydrolytic resistance tests may be grouped under two categories: hydrolytic resistance on the receptacle and hydrolytic resistance on powder. In each case, double-distilled water is placed in contact with the glass at a high controlled temperature for a predetermined time. For glass tubes, the test on powder is the only one available. The ASTM test and the various pharmacopoeias define the various protocols for the method using glass powder.

Neutral clear NSV51 and W33 glass falls under Type I, according to the definition of the various pharmacopoeias. Both glass types are highly suitable to contain injectable products in ampoules, vials, syringes and cartridges.

Viscosity

Viscosity is defined as resistance to the flow of a fluid. In glass, the viscous properties govern all aspects of melting, working and annealing of glass. As the characteristic viscosity points extend across the major part of the viscosity scale, measurements are expressed in the log of viscosity. Certain temperatures determined by their viscosity are extensively used to describe glass characteristics. The first of these points is the quenching point, corresponding to the log (viscosity) of 14.5. At this point, glass can be considered as an elastic solid. The annealing point corresponds to a log (viscosity) of 13.0. At this temperature, all thermal stresses may be quickly eliminated by cooling at 4°C/minute. The actual cooling rate will depend on the size of the article to be annealed. The Littleton point is the temperature at which a glass fibre of a thickness of 0.50 to 0.75 millimetres and 23 centimetres long will stretch at a speed of 1 millimetre/minute under the effect of its own weight. This point equates to a log (viscosity) of 7.6. The working temperature corresponds to a log (viscosity) of 4.0. At this temperature, the glass is sufficiently fluid to be worked and sufficiently viscous to retain the shape of the piece that has been produced. This viscosity point, the Littleton point and the annealing point are sufficient to describe the viscosity/temperature graph for a glass of a given composition.

Coefficient of expansion

- The coefficient of expansion measures the degree of expansion or contraction of glass as a function of temperature change.
- The linear coefficient expresses the change in length of a piece of glass when the temperature rises 1°C.
- The lower the coefficient, the better the resistance to thermal shock.
- Thus, when two pieces of glass are to be joined, their coefficients of expansion must be substantially equal.

NIPRO GLASS

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TABLE 6

TOLERANCE STANDARDS - AMPOULE (NSV 51) - AMPOULE TUBING

Outer diameter range (mm)	Thickness range (mm)	OD Tolerance (mm)	Thickness Tolerance (mm)
10.0-14.9	0.45-0.59	0.12	0.03
	0.60-0-69	0.12	0.03
15.0-17.9	0.45-0.60	0.14	0.03
	0.65-0.80	0.14	0.03
18.09-19.9	0.55-0.60	0.14	0.03
	0.65-0.99	0.18	0.03
20.0-20.9	0.55-0.60	0.19	0.03
	0.65-0.99	0.19	0.03
21.0-22.9	0.65-0.99	0.19	0.03
23.0-24.9	0.80-0.99	0.19	0.03

TABLE 8

CHEMICAL PROPERTIES

Chemical	NSV51	W33
SiO_2	74.5%	80%
Al_2O_2	745.8%	2.2%
$Na_2O + K_2O$	8%	4.1%
CaO + MgO	0.4%	0%
B_2O_3	11.3%	13.7%
BaO	<0.1%	0%
CeO_2	<0.1%	<0.1%
Traces	<0.3%	<0.3%

- As a general rule, expansion is measured between 0 and 300°C.

Density

- Density is an important property of glass, used as a measure of the consistency of the manufacturing process.
- Density can easily be measured to a high degree of accuracy. Density variations may indicate changes in the chemical composition of the glass.
- By using density as a control parameter one can ensure consistency of the composition.

TABLE 7

VIAL (NSV) - VIAL (NSV 51 AND W33) - VIAL TUBING

Outer diameter range	Thickness range (mm)	OD tolerance (mm)	Thickness tolerance (mm)
6.8-8.9 (NSV 51 only)	0.80-0.95	0.10	0.03
	1.00-1.10	0.12	0.04
	1.10-1.20	0.12	0.04
	1.30-1.50	0.16	0.05
9.0-9.9 (NSV 51 only)	0.70-0.99	0.12	0.03
	1.00-1.19	0.14	0.04
	1.20-1.29	0.15	0.04
	1.30-1.50	0.19	0.05
10.0-14.9	0.70-0.99	0.12	0.03
	1.00-1.19	0.14	0.04
	1.20-1.29	0.15	0.04
	1.30-1.50	0.19	0.05
15.0-17.9	0.85-0.99	0.14	0.03
	1.00-1.09	0.14	0.04
	1.10-1.29	0.18	0.04
	1.30-1.39	0.18	0.05
	1.40-1.60	0.20	0.05
18.0-19.9	1.00-1.09	0.19	0.04
	1.10-1.35	0.19	0.04
18.0-19.9 (W33 only)	1.40-1.60	0.23	0.05
20.0-20.9	1.00-1.09	0.19	0.04
	1.10-1.35	0.19	0.04
20.0-20.9 (W33 only)	1.40-1.60	0.23	0.05
21.0-22.9	1.00-1.09	0.19	0.04
	1.10-1.30	0.19	0.04
	1.35-1.60	0.23	0.05
23.0-24.9 (W33 only)	1.35-1.60	0.23	0.05
25.0-29.9	1.00-1.09	0.19	0.04
	1.10-1.29	0.24	0.04

TABLE 9

PHYSICAL PROPERTIES

Specification	NSV51	W33
Specification	NSV51	W33
Softening point	789°C	807°C
Annealing point	569°C	557°C
Expansion (x10-7K-1)	50	32
Density (Annealed) g/cm3	2.31	2.22
Strain point	522°C	507°C

TEST ON USP POWDER

Hydrolytic resistance test European pharmacopoeia
Receptacles for injection Japanese pharmacopoeia
ISO 719
DIN 12 116
ISO 695

TYPE 1

Type 1
Compliant
HGB 1
ACID class 1
Class A2