Specifications

Vials and bottles for parenteral application:

- **Injectables**
- **Infusions**

Approval cycle

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Acceptance of the specifications

Additional Agreement to the specifications: Yes ☐ No ☐ Number of pages:

Signature of the Specifications:

For the company:

NAMES	FUNCTIONS	DATES	SIGNATURES

For SGD Pharma: Internal classification number:……

NAMES	FUNCTIONS	DATES	SIGNATURES

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1. Introduction

As specified in the European Pharmacopoeia, the manufacturer of a pharmaceutical product is responsible for ensuring the suitability of the chosen container.

According to their hydrolytic resistance, glass containers are classified as follows:

- Type I glass container: neutral glass, with a high hydrolytic resistance due to the chemical composition of the glass itself,
- Type II glass container: usually of soda-lime-silica glass with a high hydrolytic resistance resulting from suitable treatment of the surface,
- Type III glass container: usually of soda-lime-silica glass with only a moderate hydrolytic resistance.

SGD Pharma is one of the main manufacturers of moulded glass vials and bottles for pharmaceuticals, product quality is a major aspect of its policy.

This can particularly be seen in:

- **The specialization of its production lines,**
- **Considerable capital outlays,**
- **Cleanliness policy (reflected in particular in its clean rooms),**
- **The training and involvement of all staff,**
- **A Quality Management System ISO 15378 certified, based on the Good Manufacturing Practice of the pharmaceutical industry,**
- **An ongoing improvement policy focused on customer satisfaction.**

Under this policy, the present Specifications for parenteral application vials and bottles are designed to optimize relations between the customer and the supplier. Any industrial manufacturing process implies an agreement between the customer and its supplier in terms of product quality levels.

These Specifications for parenteral application vials and bottles define the minimum quality level considered as acceptable by our customer, and the methods used to inspect this minimum quality level.

The aim of these Specifications for parenteral application vials and bottles is thus to define the acceptable quality standards by non-conformity category for the following bottles:

Vials and bottles for:

- **Liquid injectables**
- **Powder injectables**
- **Freeze dried injectables**
- **Infusion**

Additionally, to these Specifications for parenteral application vials and bottles SGD Pharma has defined in a Quality Agreement the quality requirements to be followed with regard to the manufacturing, testing and quality assurance operations of the products.

2. General conditions

Above and beyond these Specifications for parenteral application vials and bottles, SGD Pharma undertakes to pursue its efforts to improve its manufacturing process and inspection methods in compliance with its quality assurance approach and the Good Manufacturing Practice of the pharmaceutical industry.

These Specifications for parenteral application vials and bottles are the property of SGD Pharma. The information contained herein as well as all information regarding processes, materials and inspection methods made available to our customers during discussions shall be treated as confidential. Our customers thereby undertake not to disclose any of the aforementioned information to any third party whatsoever.

The SGD Pharma Specifications apply to all standard vials and bottles manufactured by SGD Pharma. They may apply, after approval from our customers, to speciality vials and bottles.

As part of its Quality Assurance approach, SGD Pharma will update these General Specifications to reflect the changing needs of the various market segments.

All inspection measures taken to ensure quality complies with these Specifications for parenteral application vials and bottles, do not imply a transfer of responsibility.

3. General Specifications

3.1. Compliance with pharmacopeias

For glass vials and bottles, these requirements basically relate to:

- Hydrolytic resistance,
- Light transmission (for amber glass).
- Arsenic

SGD Pharma manufactures its pharmaceutical vials and bottles in compliance with the requirements of European and American pharmacopoeias.

This implies:

- Upstream from the process, a rigorous selection of raw materials and appropriate glass compositions,
- Downstream from the process, inspections ensuring the result obtained.

The non-compliance of any one of the above parameters is considered to be a class A non-conformity (see § 4).

The pharmaceutical vials and bottles manufactured and commercialized by SGD Pharma are in compliance with:

- Monograph 3.2.1 Glass container for pharmaceutical use of the current European Pharmacopoeia,
- Chapter <660> Container – Glass of the current US pharmacopoeia.

3.2. Production environment / Clean Room

In order to limit the risk of contamination, the “cold end” (downstream part of the production line where production inspection and packing takes place) are located in rooms with controlled atmosphere.

The particle rate in the air is regularly measured to ensure that this room always complies with class ISO 8 of ISO Standard 14644-1. This class corresponds to class 100 000.

3.3. Packaging waste / Heavy metals

The sum of the levels of concentration of lead, cadmium, mercury, and hexavalent chromium present in SGD Pharma bottle glass is less than 100 ppm by weight (see Directive 94/62/CE on packaging waste – Article 11).

3.4. Compliance with TSE / BSE

The raw or sourced materials or reagents used in the manufacturing process are not derived from animals or humans and thus comply with EMA/410/01.

3.5. External surface treatment

Hot and cold surface treatments applied to the external surface of the vials and bottles improve its mechanical resistance, and so reduce the risk of breakage on the processing/packing line.

It also reduces the risk of scratching and facilitates vials and bottles flow on the processing/packing line (improved bottle « slide »).

It is for this reason that SGD Pharma generally recommends this type of treatment.

To avoid contamination of the internal surface of the vials and bottles, SGD Pharma systematically uses:

- A so-called « neck finish protection » device for hot treatment,
- A spray treatment between rows for cold treatment.

3.6. Vials and bottle production drawing

For each product, there is an existing Technical Drawing stating the main dimensions and overflow specification.

For speciality products, the customer must approve the drawing by writing prior to production launch.

The dimensions subject to inspection are those indicated with a tolerance on the drawing. Reference to standard (ISO, CETIE ...) are indicated on the drawing applicable to the article.

The approximate weight on the technical drawing is only indicative, only the capacity is considered as a technical specification.

3.7. Packaging Palletization

SGD Pharma packs the vials and bottles inside a shrink-wrap plastic film (with a welded sealing) usually called “packs”, directly on the production line.

Other types of packaging are available on customers request.

The packing and palletization specifications are defined and summarized in packing specification sheets that can be supplied to our customers on request.
Standard packaging for the product is as follow:

- A wooden pallet in compliance with the standard ISPM 15 and the dimensions indicated in the packing specification sheets,
- A plastic foil is inserted between the pallet and the product packed in welded plastic packing
- The number of vials and bottles by unit of packs and by layers are specified in packing specifications sheets
- A divider is inserted between each layer
- A shrink-wrap film maintains the vials and bottles on the pallet.

3.8. Vials and bottles shelf life

The shelf life of the vials and bottles Type I, Type II and Type III is at least 6 years from the date of manufacturing date.

3.9. Vials and bottles storage

Storage time will depend upon humidity and temperature in the storage place. These are the most influential parameters in the natural process of glass exudation. Aging in the presence of moisture and temperature changes can result in the migration of alkali elements (Na_2O) present in the glass on its surface. This presence often takes the form of a whitish bloom.

At SGD Pharma the pallets of vials and bottles are stored inside a warehouse. In there, a rodent control program is in place. The temperature inside, is similar to the outside temperature, the warehouse insulation prevents big temperature variations.

The pallets are stackable on a five-meters maximum height, unless otherwise specified.

3.10. Ready for use statement

As described in this SGD Pharma Standard Specifications for oral and nasal application vials and bottles listed hereabove, SGD Pharma implemented the following in order to limit the risk of contamination: final product inspection in Clean Rooms ISO 8 (100 000), and clean room environment monitoring for particles as per ISO 14644.

Additionally, turn and blow equipment is in place at the end of all cold end lines within the clean rooms ISO 8 (100 0000), clean room environment is also monitored for microbiological contamination as per internal procedures and adequate controls are in place to detect non-conforming products.

The products manufactured under the aforementioned specifications are hence ready for use with limited risks. Nevertheless, it is not possible to offer absolute warranty of non-contamination due to product handling, loading unloading and transportation of the bottles.

As a consequence, it is the responsibility of our customers to ensure that the risk to the patient or to the consumer is fully assessed and that adequate validation was done and internal controls are in place.

3.11. Labelling – Traceability

All pallets are labelled.

The details on each label will identify:

- SGD Pharma item code (10 digits)
- Packing characteristics:
  - Number of items by box (number of module)
  - Number of boxes by layer
  - Number of layers by pallet
  - Number of items by pallet
- Batch number identifying:
  - the plant where it was manufactured
  - the year of manufacturing
  - the serial number within this year
- The pallet number

When using vials and bottles, it is important to keep the pallet labels, since in case of a problem, the data on the labels can be used to track back to the production and inspection parameters.

A sample pallet label is enclosed to the present General Specifications (Appendix 2).

3.12. Batch / lot definition

During production at SGD Pharma:

Each lot corresponds to vials and bottles manufactured consecutively on the same machine; it is thus a homogeneous batch. (Also called production run).

Certificates of Quality are issued on this same basis, i.e. each certificate corresponds to a single batch, (Appendix 3).

On delivery to the customer, each SGD Pharma shipment for a given item number and a given SGD Pharma batch number constitute an in-coming inspection batch.

3.13. Compliance certificate

As part of its quality assurance, SGD Pharma systematically issues Certificates of Quality attached to each delivery.

These certificates are related to a complete production batch. They certify the application of inspection procedures and the compliance of the products to the present Specifications.

The issue of such certificates in no way exempts the customer from its responsibility under common law.

Two samples of the certificates are enclosed to the present Specifications (Appendix 3).

3.14. Quality level – A.Q.L. / Choice

The level of quality is defined as follows:

- According to criticity, the non-conformities are ranked by class; each class is associated with a defined Acceptance Quality Limit (cf. NF ISO 2859-1).
- Imperfections, if their size does not exceed a certain threshold, will not be considered as a non-conformity. These thresholds are defined in Appendix 1; they are associated with what we call the « standard choice of vials and bottles for oral pharmaceutical products ».

On customer's request, SGD Pharma can apply different choices level, which will impact the selling price. (Cf. Appendix 1).

4. Statistical quality control

4.1. Statistical quality control method

Inspection is conducted by attributes, i.e. counting the non-conform vial as a non-conformity.

- As explained above: the non-conformities are ranked by class; each class is associated with a defined Acceptance Quality Limit.

The inspection is carried out in compliance with the sampling schedules of ISO standard 2859-1.

- The ISO standard 2859-1 tables used are the following:

- Table 1 with inspection level II or S3 to determine the sample code letter
- Table 2A (simple sampling plan – normal inspection) to determine the acceptance threshold as
  a function of the sample letter code and the A.Q.L.

- Inspection batch: see § 3.11

The bottles are sampled randomly from a number of pallets/packs equal to the square root of the total number of pallets/packs in the batch to be inspected.

The following table summarizes the sampling and decision rules for Level II normal inspection.

Batch size	Sampling		A.Q.L 0,40		A.Q.L 0,65		A.Q.L 1,5		A.Q.L 4	
N	N		A	R	A	R	A	R	A	R
3 201 / 10 000	L	200	2	3	3	4	7	8	14	15
10 001 /35 000	M	315	3	4	5	6	10	11	21	22
35 001 / 150 000	N	500	5	6	7	8	14	15	*27*	*28*
150 001 / 500 000	P	800	7	8	10	11	21	22	*41*	*42*
> 500 000	Q	1250	10	11	14	15	*26*	*27*	*61*	*62*

NB: The figures in *underlined italics* do not appear in the tables in ISO Standard 2859 -1; but they have been calculated using the same method.

Sheet of sampling S3

Batch size	AQL 0,010	AQL 0,015	AQL 0,025	AQL 0,040	AQL 0,065	AQL 0,10	AQL 0,15	AQL 0,25	AQL 0,40	AQL 0,65	AQL 1,0	AQL 1,5	AQL 2,5	AQL 4,0
501 - 3 200	Prel. 1250 A : 0 R : 1	Prel. 800 A : 0 R : 1	Prel. 500 A : 0 R : 1	Prel. 315 A : 0 R : 1	Prel. 200 A : 0 R : 1	Prel. 125 A : 0 R : 1	Prel. 80 A : 0 R : 1	Prel. 50 A : 0 R : 1	Prel. 32 A : 0 R : 1	Prel. 20 A : 0 R : 1	Prel. 13 A : 0 R : 1	Prel. 8 A : 0 R : 1	Prel. 20 A : 1 R : 2	Prel. 13 A : 1 R : 2
3 201 - 35 000											Prel. 20 A : 0 R : 1	Prel. 32 A : 1 R : 2		Prel. 20 A : 2 R : 3
35 001 - 500 000											Prel. 50 A : 1 R : 2		Prel. 32 A : 2 R : 3	Prel. 32 A : 3 R : 4
> 500 000										Prel. 80 A : 1 R : 2		Prel. 50 A : 2 R : 3	Prel. 50 A : 3 R : 4	Prel. 50 A : 5 R : 6

4.2. Method for counting non-conformities

The number of faulty bottles of each class is calculated according to the following rules:

- If a same bottle has several non-conformities, it is only counted once; if the non-conformities belong to different classes, it is the lowest A.Q.L. that counts.
- For finished bottles, the glass and finishing non-conformities in the same class are considered cumulatively.

4.3. Definition of non-conformity classes and corresponding A.Q.L.

The non-conformity classes are the following:

- Class A non-conformities or A critical non-conformities.
- Class B non-conformities or B critical non-conformities.
- Class C non-conformities or C major non-conformities.
- Class D non-conformities or D major non-conformities.
- Class E non-conformities or E aspect non-conformities.

* **Class A non-conformities or A critical non-conformities** **A = 0 R = 1**

These bottles represent a risk for users.
If a non-conformity of this class is found during the delivery inspection, the inspected batch is rejected.

The A.Q.L. corresponding to A=0 R=1 varies as a function of the sample, which depends on the size of the batch to be inspected. The A.Q.L. are summarized in the following table:

Table giving the A.Q.L. for A = 0 R = 1	
Sample size	A.Q.L.
125	0,10
200	0,065
315	0,040
500	0,025
800	0,015
1250	0,010

Note:
Despite many measures aiming at ensuring a very high-quality level to its products, SGD Pharma is unable to guarantee absolute zero non-conformities.
Consequently, the A=0, R=1 rule should be used only for statistical quality control.
The discovery of a bottle with a class A non-conformity on the production line, does not automatically result in the rejection of the batch (the rejection would only be justified if, in the absence of a statistical quality control at delivery, an inspection is carried out later and reveals the presence of a significant number of bottles with this class non-conformity).

* **Class B non-conformities or B critical non-conformities**

These non-conformities are liable to serious disruption of the customer process line.

The A.Q.L. for this class is 0,4

* **Class C and D major non-conformities**

These non-conformities, despite being not critical, might cause failure or significantly reduce the product intended use.

Depending on the impact, they are classified as major C or major D non-conformities:

- **Class C non-conformities or C major non-conformities**

The A.Q.L for this class is 0,65

- **Class D non-conformities or D major non-conformities**

The A.Q.L for this class is 1,5

* **Class E non-conformities or aspect non-conformities**

These non-conformities reflect a disparity versus specifications, but which do not jeopardize the use of the product.

The A.Q.L. for this class is 4

5. Categories of non-conformities

Non conformités	Inspection levels		Non-conformities
Classe = A ou Critiques A	**II**	**S3**	**Class = A or Critical A**
A = 0 **R = 1**			**A = 0** **R = 1**
Aiguille	x		Spike
Bouillon cassant intérieur (1)	x		Internal soft blister (1)
Débris de verre intérieur	x		Adhered glass particle
Ailette coupante	x		Sharp dangerous fin
Non-conformité bague avec non-étanchéité (pli sur bague, bague mal rendue)	x		Finish distortion affecting sealing integrity: (line over finish unfilled-malformed finish)
Erreur de gravure	x		Incorrect engraving
Incisé traversant (*) coupé bague	x		Split finish (*)
Incisé traversant (*) bas col	x		Crack at base of the neck (*)
Incisé traversant (*) corps	x		Crack on the Body (*)
Incisé traversant (*) fond	x		Crack at the bottom (*)
Mélange de flacons (bague ou fond)	x		Rogue component (neck or bottom)
Perchoir/ trapèze	x		Bird swing
Choqué avec perte d'étanchéité	x		Bump check integrity affected
Picot intérieur	x		Inside projection
Résistance hydrolytique non conforme aux exigences des pharmacopées européenne et américaine		x	Non-conforming hydrolytic resistance (in reference to European and American pharmacopeia)
Transmission lumineuse non conforme aux exigences des pharmacopées européenne et américaine (verre jaune uniquement)		x	Non-conforming spectral / light transmission (in reference to European and American pharmacopeia - amber glass only)
(1) Voir aussi l'annexe 1 (*) ou glaçure avec perte d'étanchéité			(1) Refer to appendix 1 (*) Affecting sealing integrity

Non conformités	Inspection levels		Non-conformities
Classe = B ou Critiques B	**II**	**S3**	**Class = B or Critical B**
N.Q.A. 0,40			**A.Q.L. 0.40**
Incisé non traversant bague	x		Check in the neck
Incisé non traversant bas col	x		Check at base of the neck
Incisé non traversant corps	x		Check on the body
Incisé non traversant fond	x		Check at the bottom
Bavure intérieure bague	X		Neck finish inside over press
Cassé sans morceau de verre	x		Breakage without glass in packaging
Débris de verre libre			Lose glass
Corps étrangers intérieurs visibles	x		Internal, visible foreign bodies
Déformation grossière affectant l'utilisation	x		Severely deformed not suitable for processing
Diamètre corps ou bague > maxi		x	Body or neck diameter > maxi
Diamètre Intérieur Col < mini		x	Bore diameter < mini/ Choked neck
Diamètre ouverture hors tolérance		x	Neck ID out of tolerance
Dimension hauteur > maxi		x	Overall height > maxi
Taché intérieur non lavable (1)	x		Internal and non-removable contamination (1)
	x		
Résistance à la pression interne hors tolérance (si spécifiée)		x	Non-conforming internal pressure resistance (if specified).
Résistance à la charge verticale hors tolérance (si spécifiée)		x	Non-conforming vertical load resistance (if specified).
Recuit non conforme		x	Residual stress
<u>Pour les flacons siliconés</u> :			<u>For siliconized bottles</u>:
Siliconage non conforme selon MO 8 0003 et MO 8 0004		x	Non-conforming siliconization according to MO 8 0003 and MO 8 0004
(1) Voir annexe 1			(1) Refer to appendix 1

Non conformités	Inspection levels		Non-conformities
Classe = C ou majeurs C	**II**	**S3**	**Class = C or major C**
N.Q.A. 0,65			**A.Q.L. 0.65**
Bague ébréchée, étanchéité bonne	x		Chipped neck finish, sealing integrity non-affected
Bavure extérieure bague	x		Over press on outside of finish
Capacité ras bord < mini		x	Brimfull Capacity < mini
Déformé bague et col	x		Unfilled finish, warped finish, seal integrity is intact, pinched neck
Diamètre extérieur col > maxi		x	External diameter of neck > maxi
Fond enverré important	x		Severe glazed bottom
Paroi mince affectant la solidité	x		Thin wall thickness affecting strength of the bottle.
Taché intérieur lavable (1)	x		Removable internal contamination (1)
Marque de plongeur			Plunger mark
Test choc thermique non conforme		x	Non-conforming thermal shock
(1) Voir annexe 1			(1) Refer to appendix 1

Non conformités	Inspection levels		Non-conformities
Classe = D ou majeurs D	**II**	**S3**	**Class = D or major D**
N.Q.A. 1,5			**A.Q.L. 1.5**
Affaissé/ basculant	x		Rocker bottom
Diamètre corps et extérieur bague < mini		x	Body diameter and neck OD < mini
Dimension hauteur < mini		x	Overall height < mini
Déformé corps	x		sunken side; bulged side malformed shoulder
Ebréché	x		Chipped glass
Gravure illisible	x		Illegible engraving
Larme (1)	x		Knot (1)
Pierre (1)	x		Stone (1)
Capacité ras bord > maxi		x	Brimfull Capacity > maxi
Verticalité, bague déportée, bague penchée hors tolérance (voir fiche CETIE DT 15.04)		x	Leaner, offset neck; bent neck (see CETIE data sheet DT 15.04)
(1) Voir annexe 1			(1) Refer to appendix 1

Non conformités	Inspection levels		Non-conformities
Classe = E ou Mineur E	**II**	**S3**	**Class = E or aspect E**
N.Q.A. 4			**A.Q.L. 4**
Bague encrassée	x		Rough finish
Bouillons dans la masse (1)	x		Hard Blister
Bouillons cassant externe (1)	x		External soft blister
Puce	x		Seed
Calciné	x		Surface check
Arraché, plis creux (1)	x		Tear, hallow fold, pressure fold (1)
Choqué sans perte d'étanchéité	x		Bump check non-impacting integrity
Collé non coupant	x		Stuck glass without sharp edges
Corde/ griffure	x		Cord/ feeder streak
Fond enverré	x		Glazed bottom
Frisé (1)	x		Washboard, brush marks (1)
Martelé	x		Hammered effect
Point noir (1)	x		Black spot (1)
Pli (1)	x		Lap mark, body fold or loading mark (1)
Piqué encrassé	x		Pitted surface, orange peel
Raccord moule	x		Blank seam, mismatched neck ring seam; heavy mould seam
Raccord fond ébaucheur déporté	x		Swung baffle
Rayé	x		Scratch; scuff
Répartition irrégulière, talon	x		Heel tap
Taché extérieur (1)	x		External contamination (1)
Marque de ciseaux	x		Shear mark
<u>Pour les flacons siliconés</u> : Traces blanches de silicone Voile de siliconage	 x x		<u>For the siliconized bottles</u>: White traces of silicone Bloom of silicone
(1) Voir annexe 1			(1) Refer to appendix 1

6. Dispute settlement

This chapter details the procedure for accepting or rejecting deliveries.

6.1. Incoming inspection

Accepting or rejecting of the vials and bottles are based on statistical sampling results as described in § 4.1

Acceptance

Deliveries that pass the inspections as defined in these Specifications are accepted.

Within a continuous improvement approach, when a delivery sample has a total number of faulty units below the rejection threshold, and the customer still wants to draw SGD Pharma 's attention to the non-conformities /imperfections observed, an "annotated acceptance" is issued for delivery.
When a delivery sample has a total number of faulty units above the acceptable quality level as defined in the Specifications and if the customer deems that, exceptionally, the nature of the non-conformities or their effects on the packing process and brand image will not be too serious, this delivery can be accepted under concession.

Rejection

When the delivery does not comply with the standards defined in the Specifications, it is rejected (except in the case described in § 6.1.1 where the customer accepts the delivery under concession). A claim should be forwarded to SGD Pharma.

SGD Pharma reserves the right to carry out its own inspection.

SGD Pharma shall be advised in written. The necessary information (see § 6.3) and contentious samples should be sent to SGD Pharma as soon as possible along with the relevant traceability elements (pallet labels, certificate of compliance).

6.2. On the customer processing / packing line

This procedure relates to batches used on the customer processing/packing line without systematic delivery inspection.
In the event of an incident on the processing/packing line attributable to the bottle, the batch compliance to the Specifications should be verified.
The customer should carry out a statistical inspection in compliance with the Specifications on the remaining empty bottles from the same delivery.

If it is not possible to carry out this inspection, the percentage of non-conformities required to assess compliance with the Specifications shall be calculated on a number of bottles equal to the sample number of finished products that the customer must inspect to validate its own production.
SGD Pharma recommends a final statistical inspection approximately every two hours.

If the non-conformities are found during 100% inspection on line, referred to the table 7 of ISO 2859 to make a link with the AQL.

In the event of a claim, the procedure for returning the stock of empty bottles and processing them in order to reach the required standards is the same as that set out in § 6.1.2.

6.3. Claims procedure

To handle a claim, the customer must supply to SGD Pharma the following information:

For every complaint:

- Product reference and batch number
- Impact for customer
- Non-conformities description with pictures or samples
- Type of non-conformity (Critical, major, minor) and consequence on the filling line
- Delivery note, Invoice reference or Delivery date
- Samples (10 samples per non-conformity if possible).
- Quantity with non-conformity or non-conformity rate
- Total quantity of the batch (delivered)
- When the non-conformity has been observed:
    - at receiving:
    - at incoming inspection control:
    - during production:
    - other (please specify)
- Requested actions and lead-time constraints

Optional, but very important for traceability:

- Customer Complaint number
- Pallet labels
- Cavity number

In case of packaging/ transport issue:

- Quantity (vials or packs)
- Positions of the damaged packs on the pallet
- When it has been detected (receiving/incoming inspection)

7. Inspection methods

7.1. Dimensional inspection

This inspection is made using appropriate measurement apparatus (sliding calliper, comparator, etc…) or size gauges.

7.2. Capacity

The capacity tolerance is defined on the drawing.

Brimfull (or gauge line) capacity is measured by weighing (difference in weight between the bottle filled with water and the empty bottle).

7.3. Annealing

Annealing tension is checked using ASTM Standard C148. The delay should not exceed 18 nm per mm of glass thickness.

7.4. Hydrolytic resistance

Hydrolytic resistance is checked using the methods described in the current European and American pharmacopoeias.

7.5. Light transmission of amber glass

Light transmission is checked using the methods described in the current European and American pharmacopoeias.

7.6. Arsenic

Arsenic is checked using the methods described in the current European and American pharmacopoeias.

7.7. Strength tests

If specified, internal pressure resistance is checked using ISO 7458 Standard (AGR's « Ramp Pressure Tester » measures in compliance with this standard).

If specified, vertical load resistance can be measured using ISO 8113 standard.

7.8. Resistance to thermal shock test

Resistance to thermal shocks is measured in compliance with ISO 7459 standard (limits established according to the type of glass).

8. Validity of the specifications

Once signed by both parties, the Customer and SGD Pharma, the present Specifications shall be considered valid without any time limitation

The Specifications may not be modified without the approval of both parties.

If no specific agreement is concluded with the client, our standard aforementioned specifications apply.

9. Appendices

Appendix 1: Maximum size of acceptable non-conformities / imperfections in standard choice of Vials and bottles parenteral application
Appendix 2: Pallet label
Appendix 3: Certificate of Quality
Appendix 4: Summary of changes

Appendix 1

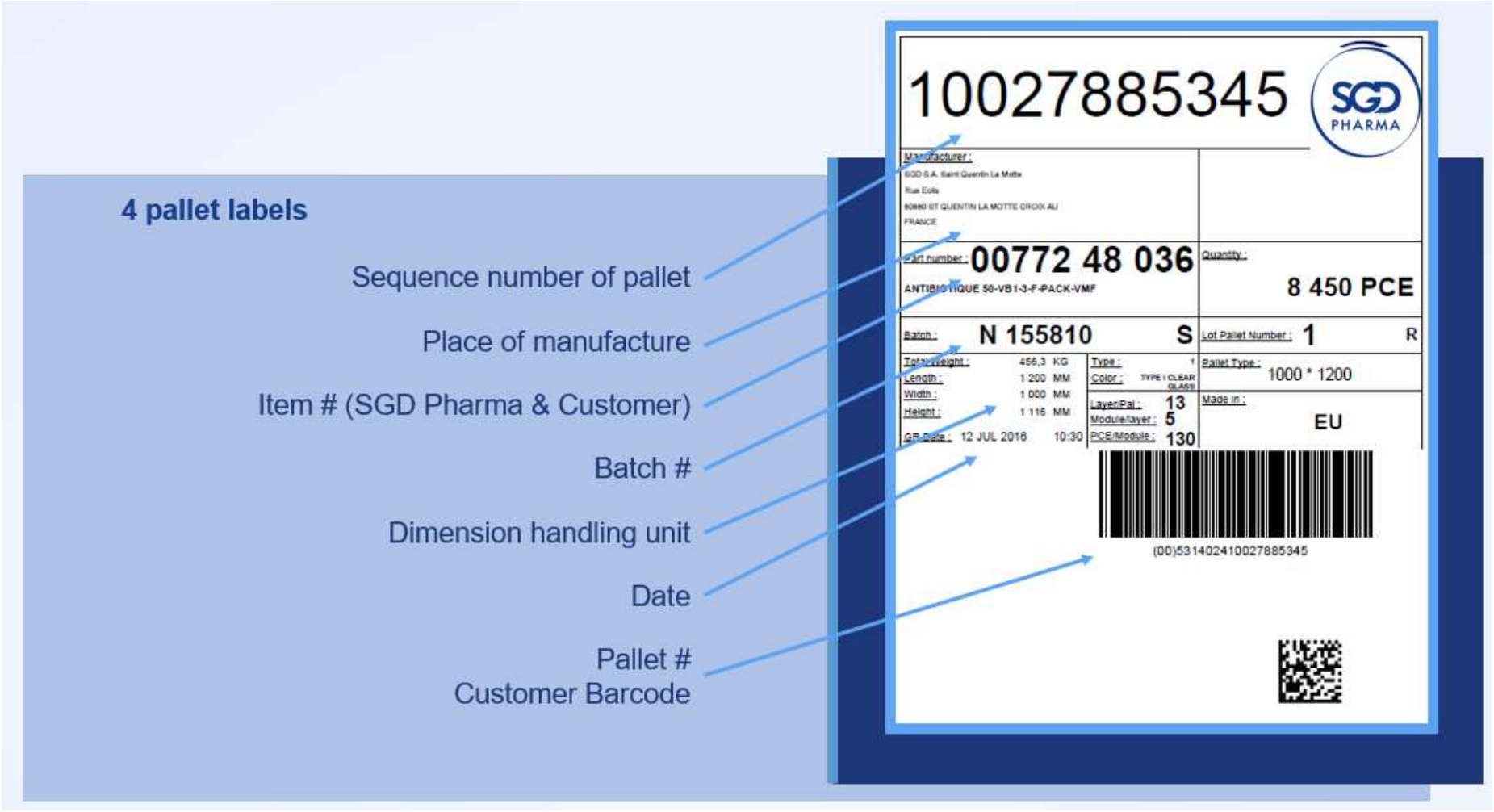
Maximum size of acceptable non-conformities / imperfections in standard choice of Vials and bottles parenteral application

In case of an elongated blister, the dimension to be considered should be the average measurement = (length + width)/2.

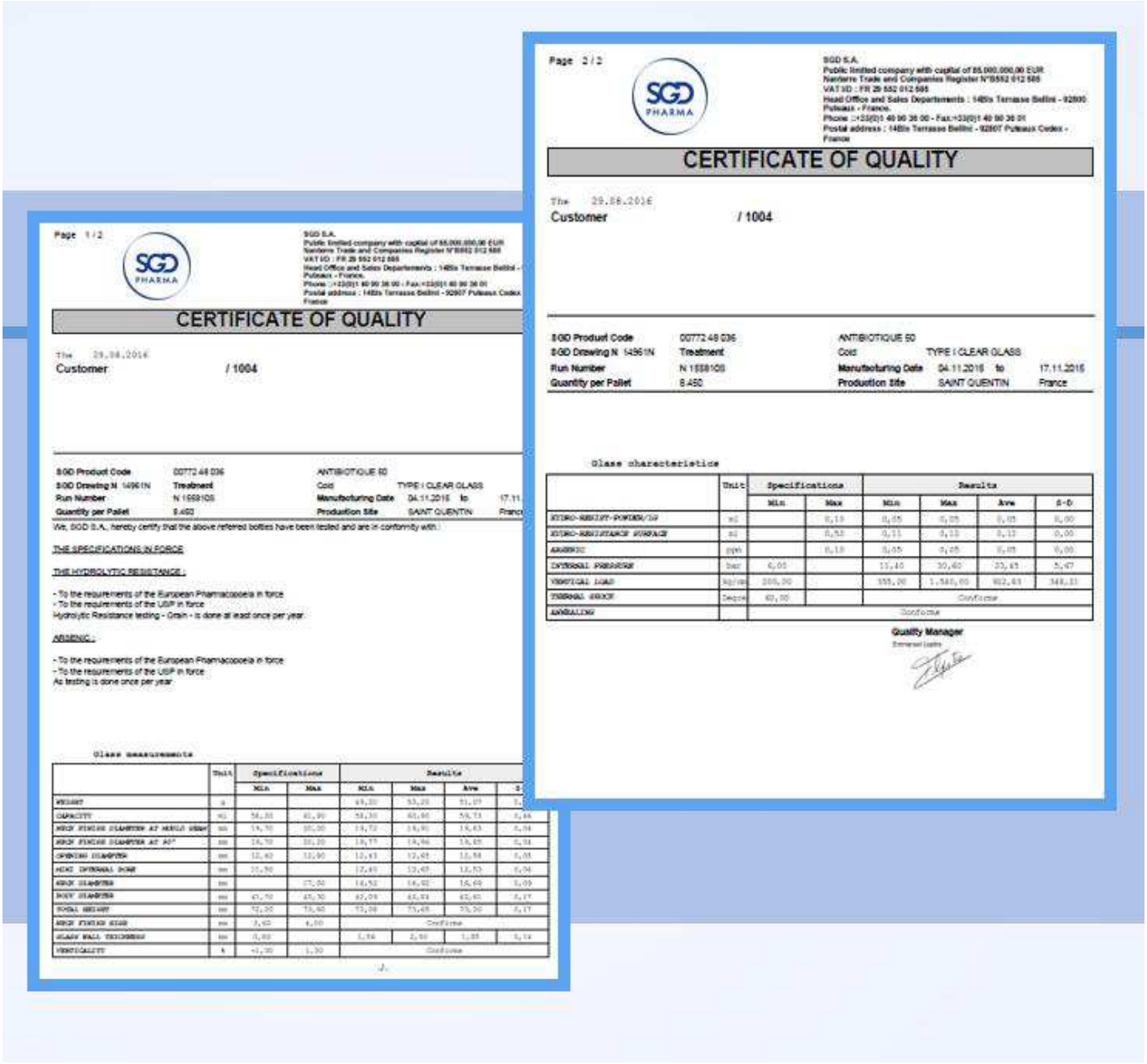
Non-conformites / Non-conformities		Choix / Choice I	Choix / Choice II	Choix / Choice P	Standard Choice SGD Pharma Choix / Choice III
Bouillon dans la masse	Blister	1,3 mm	1,5 mm	1,8 mm	2,5 mm
Bouillon de surface externe Bouillon creux externe	External skin blister External Soft Blister	0,8 mm	1,0 mm	1,5 mm	2 mm
Bouillon de surface interne Bouillon creux interne	Internal skin blister Internal Soft Blister	0,8 mm	0,8 mm	0,8 mm	0,8 mm
Larme	Knot	0,8 mm	1 mm	1,5 mm	2 mm
Pli corps / arraché	Body fold or lap / tear	1 cm	1,5 cm	2 cm	2,5 cm
Point noir intérieur	Black spot internal	0,5 mm	0,8 mm	1 mm	1,3 mm
Frisé	Wash Board	1 cm^2	1,5 cm^2	1,8 cm^2	2 cm^2
Taché intérieur	Internal Dirt	0,5 mm	0,8 mm	1 mm	1,3 mm
Taché extérieur	Exterior mark	0,5 mm	0,8 mm	1,0 mm	1,5 mm
Pierre/inclusion	Stone/inclusion	0,8 mm	1 mm	1,3 mm	1,5 mm

Appendix 2

Pallet label



Appendix 3
Certificate of Quality



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SGD S.A.
Public limited company with capital of 85.000.000,00 EUR
Nanterre Trade and Companies Register N°B552 012 585
VAT ID : FR 25 552 012 585
Head Office and Sales Departements : 14Bis Terrasse Bellini - 92800 Puteaux - France.
Phone :+33(0)1 40 90 36 00 - Fax:+33(0)1 40 90 36 01
Postal address : 14Bis Terrasse Bellini - 92807 Puteaux Cedex - France

CERTIFICATE OF QUALITY

The 29.06.2016
Customer / 1004

SGD Product Code	00772 48 036	ANTIBIOTIQUE 50	
SGD Drawing N 14961N	Treatment	Cold	TYPE I CLEAR GLASS
Run Number	N 1558105	Manufacturing Date	04.11.2015 to 17.11.2015
Quantity per Pallet	8 450	Production Site	SAINT QUENTIN France

Glass characteristics

	Unit	Specifications		Results			
		Min	Max	Min	Max	Ave	S-D
HYDRO-RESIST-FONDUE/IP	ml		0,10	0,05	0,05	0,05	0,00
HYDRO-RESISTANCE SURFACE	ml		0,02	0,01	0,01	0,01	0,00
ARSENIC	ppm		0,10	0,05	0,05	0,05	0,00
INTERNAL PRESSURE	bar	6,05		11,40	30,40	20,65	5,47
VERTICAL LOAD	kg/cm²	200,00		355,00	1.580,00	902,83	348,21
THERMAL SHOCK	Degré	60,00		Conforme			
ANNEALING		Conforme					

Quality Manager

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SGD Drawing N 14961N	Treatment	Cold	TYPE I CLEAR GLASS
Run Number	N 1558105	Manufacturing Date	04.11.2015 to 17.11
Quantity per Pallet	8 450	Production Site	SAINT QUENTIN Franc

We, SGD S.A., hereby certify that the above referred bottles have been tested and are in conformity with :

THE SPECIFICATIONS IN FORCE

THE HYDROLYTIC RESISTANCE :

- To the requirements of the European Pharmacopoeia in force
- To the requirements of the USP in force

Hydrolytic Resistance testing - Grain - is done at least once per year.

ARSENIC :

- To the requirements of the European Pharmacopoeia in force
- To the requirements of the USP in force

As testing is done once per year.

Glass measurements

	Unit	Specifications		Results			
		Min	Max	Min	Max	Ave	S-D
WEIGHT	g			49,30	53,20	51,07	1,1
CAPACITY	ml	58,30	61,90	58,30	60,90	59,73	0,46
HEIGHT FINISH DIAMETER AT HEIGH HEAD	mm	19,70	20,30	19,72	19,91	19,83	0,04
HEIGH FINISH DIAMETER AT 90°	mm	19,70	20,30	19,77	19,96	19,85	0,04
OPENING DIAMETER	mm	12,40	12,90	12,43	12,65	12,58	0,05
HEIGHT INTERNAL BORE	mm	10,50		12,65	13,47	12,83	0,04
NECK DIAMETER	mm		17,00	16,52	16,92	16,69	0,09
BODY DIAMETER	mm	41,70	45,30	42,04	43,83	43,01	0,17
TOTAL HEIGHT	mm	72,30	75,60	73,08	75,48	73,90	0,17
NECK FINISH SIZE	mm	2,60	4,00	Conforme			
GLASS WALL THICKNESS	mm	0,80		1,04	2,50	1,25	0,14
VERTICALITY	°	+0,30	1,30	Conforme			

Appendix 4
Summary of Changes

Section	Changes
-	Update of SGD Pharma's logo Update of document's title AQL: Acceptance Quality Limit Oral instead of drinkable Change of the word template « Non-conformities » instead of defect
Introduction	'Quality Management System' instead of 'quality assurance system' – 'General' added to 'Specifications'
3.2	Translation of the title, becomes: 'Production environment/ Clean Room' Part 1 of ISO Standard 14644 added
3.4	Clarification of this section: 'The raw or sourced materials or reagents used in the manufacturing process are not derived from animals or humans and thus comply with EMA/410/01.' Regulation EMA/410/01 added
3.5	Last sentence suppressed
3.6	First sentence suppressed
3.7	'The product is sitting on' suppressed + mention of the ISPM 15 norm
3.8 & 3.9	Divide section shelf life and storage in two 'The minimum…one year' suppressed 'Under normal….one year' added – 'The minimum storage period under normal European weather conditions will be around one year' modify by 'Under normal European weather conditions, storage period can be around one year'
3.10	'If the customer notes any damage to pallets delivered, SGD recommends raising standard reserves on the delivery notes when taking delivery.' Suppressed (to be put in the Standard QA)
3.11	'Number of modules' added 'The production line' suppressed
3.12	'The final (dedicated area)' suppressed Last sentence modified by: 'Each SGD Pharma shipment for a given item number and a given SGD Pharma P/O number constitute an in-coming inspection batch.'
3.15	Change Control section suppressed
3.16	Cleanliness section suppressed
3.17	Handling quality records section suppressed
4.1	Remove % from AQL
4.1	Correction in the sheet of sampling S3 + Add lower AQL and remove 6.5
5	Alignment on the PDA report 43
6.1.1	'Within a continuous improvement approach' added 'under concession' instead of 'with a derogation'
6.1.2	'under concession' instead of 'with a derogation' 'in written' instead of 'by fax or e-mail' 'Two courses of action are possible…measures' suppressed
6.2	'If the non-conformity is found during 100% inspection on line, referred to the table 7 of ISO 2859 to make a link with the AQL.' added

Section	Changes
6.3	Claim Procedure section aligned with the Standard Quality Agreement
6.4	Claim Response period section suppressed
7.3	Change from ASTM Standard C148 – 95 to ASTM Standard C148
8	Product Related Services section suppressed totally (8.1 8.2 8.3 and 8.4) and replaced by Validity of Specifications section
10	Audits section totally suppressed
Appendix 1	Add of all SGD Pharma choice
Appendix 2	New Label with new LOGO added
Appendix 4	Summary of the change added