Pre-qualification of single-use injection devices under the PQS system: A guideline for manufacturers

June 2005

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Glossary

AD	Auto-disable (syringe)
ATT	Access to Technologies (WHO team of Immunization, Vaccines & Biologicals Department)
EU	European Union
EXW	Ex Works (Incoterm)
GHTF	Global Harmonization Task Force
GMP	Good Manufacturing Practices
IAPSO	Inter-Agency Procurement Services Office (UN agency)
ISO	International Standards Organization
PIS	Product Information Sheets
PQS	Performance, Quality, Safety
QA	Quality Assurance
RPF	Reuse-Prevention Feature
UN	United Nations
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
WHO	World Health Organization

Refer to Annex 5.1 for definitions of words and phrases highlighted in blue.

1.0 Introduction

This guideline tells you how to make an application to WHO for the pre-qualification of single-use injection device for procurement by UN agencies. Under the WHO's new PQS system, you may offer devices designed either for preventive or for therapeutic purposes, provided they comply with the requirements set out in this guideline. The document describes what pre-qualification means, it gives a step-by-step guide to the pre-qualification process, and it outlines how your pre-qualified status can be maintained and also how it can be lost.

2.0 Background

In order to achieve effective infection control for intradermal, subcutaneous and intramuscular needle injections, WHO recommends the use of single-use injection devices. Single-use injection devices include single-use syringes used in conjunction with single-use needles, auto-disable (AD) syringes originally designed specifically for immunization, and syringes with a reuse-prevention feature for general purpose. In support of these recommendations, UNFPA, UNICEF and WHO have stated that, by the end of the year 2003, all countries should only use auto-disable (AD) syringes for immunization[1].

A secure supply of single-use injection devices is essential in order to reduce the infection risks associated with the reuse of injection devices in the therapeutic and preventive health care services. Security of supply depends upon effective forecasting, financing and supply management; the primary measure of effectiveness is that continuous and sustained supplies of high quality injection devices reach each and every health care facility.

The World Health Organization (WHO) and other United Nations (UN) agencies have a role to play in this process when they act in the areas of policy making, setting product specifications, and when they procure on behalf of developing countries.

The role of the medical device industry is to provide a reliable stream of safe, affordable, high quality devices designed to meet the needs and constraints of the developing world.

3.0 Procedural guide

3.1 What is the PQS system?

Since 1979 WHO, in collaboration with UNICEF Supply Division, have developed and maintained a series of performance specifications and test procedures for

[1] World Health Organization. WHO-UNICEF-UNFPA Joint statement on the use of auto-disable syringes in immunization services, 1999. WHO document WHO/V&B/99.25. Available from URL: http://www.who.int/vaccines-documents/DocsPDF99/www9948.pdf

injection devices, cold chain equipment and other immunization-related products. Products that conform to these specifications and test procedures are listed in the WHO/UNICEF *Product Information Sheets* (PIS)[2]. In the quarter of a century since it was first introduced the PIS has become the principal source of information and advice for those responsible for purchasing products for use in immunization programmes.

The PIS system is now being updated and re-launched as the PQS (Performance, Quality, Safety) system. All existing PIS performance specifications and test procedures are currently under review and new PQS-compatible documents will be published during 2004 and 2005. In addition to covering immunization-related equipment, the new system has been extended to include devices used for therapeutic purposes.

The PQS system will evaluate products and devices against the new documents; those that conform will immediately be listed as pre-qualified products on the on-line database and in the next edition of the hardcopy catalogue. Until the PQS database is up and running follow the New Items link at http://www.who.int/vaccines-access/vacman/pis/new%20sheets%20intro.htm.

3.2 Transitional arrangements for syringes for fixed dose immunization and syringes with a reuse prevention feature

By the 30 June 2005 single-use injection devices previously listed in the PIS will, in principle, no longer be procured by United Nations agencies unless the new pre-qualification procedure, described in this document, has been completed. Under the new procedure, auto-disable (AD) syringes for fixed dose immunization shall comply to ISO standard 7886 - part 3, (issued 1 march 2005). Syringes with a reuse prevention feature shall comply with ISO-DIS 7886- part 4 (ISO/TC 84/SC 1).

3.3 Pre-qualification of syringes for general purpose use

In the first stage of implementation of the PQS only AD syringes for fixed dose immunization and syringes with a reuse-prevention feature will be prequalified under the PQS system. The PQS Steering Group will, in consultation with partners and industry consider the prequalification of therapeutic single-use devices and insulin injection devices in July 2006 (one year from the date of PQS for injection devices introduction).

3.4 What does PQS pre-qualification mean?

As noted in paragraph 3.2, injection devices currently listed under the PIS system will, in principle, not longer be purchased by UN procurement agencies after 30 June 2005, unless they have been pre-qualified under the PQS system.

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[2] The 2000 edition of the *Product information Sheets* can be downloaded from the WHO website at: www.who.int/vaccines-documents/DocsPDF00/www518.pdf and new items added since this publication are available at http://www.who.int/vaccines-access/vacman/pis/new%20sheets%20intro.htm

The granting of PQS pre-qualification status does not constitute a guarantee of purchase. Pre-qualification indicates only that the device is technically satisfactory for procurement by United Nations Agencies for the purpose for which it is intended, and subject to any limitations set out in the PQS database or catalogue. You, as the manufacturer of the device, are entirely responsible for making a commercial arrangement with a potential purchaser and for ensuring that the quality of the delivered device is acceptable to that purchaser. Technical specifications shall not be in contradiction to the established ISO standards. In this context the word 'purchaser' can mean any one of the UN agency procurement units, including UNICEF, IAPSO, UNFPA, and WHO.

3.5 What products are eligible for pre-qualification?

Devices that conform to one of the two categories described in this section are potentially eligible for pre-qualification. Compliance with one of the two listed ISO standards is mandatory. Devices that only conform to national or regional standards are *not* eligible even if they do comply with the licensing and/or quality system standards set out in section 3.6. These are the three categories:

Category 1: Syringes for therapeutic use:

Syringes for general purpose use with a reuse-prevention feature must satisfy the requirements of *ISO/DIS 7886- part 4.*

Category 2: Syringes for fixed-dose immunization:

- Auto-disable syringes for fixed dose immunization must satisfy the requirements of ISO 7886- part 3.

Category 3: Syringes for insulin injection:

- Syringes for insulin injection must comply with ISO 8537.

Hypodermic Needles: The needles for all ISO-compliant devices must conform to ISO 7864.

Generally: You should be aware that the individual UN procurement agencies reserve the right to impose additional conditions when seeking offers for the supply of pre-qualified syringes. The technical specifications shall not be in contradiction to established ISO standards.

Note: at this stage, this pre-qualification procedure is geared towards syringes, there is no separate category covering hypodermic needles. This may be covered at a later stage.

3.6 What are the minimum licensing requirements?

If a device is licensed in the territory of one of the founding members of the Global Harmonization Task Force (GHTF)[3], it meets the minimum quality criteria required under the PQS pre-qualification procedure (Option 1 below). If the device is *not*

[3] The founding members of the GHTF are Australia, Canada, the European Union, Japan and the United States.

licensed, you must be able to demonstrate to us that your manufacturing process meets one or more of the quality system standards listed below (Option 2).

1. **Option 1: License in a GHTF founding member country:** Domestic market clearance in any one of the five countries will indicate to us that you have an acceptable quality system in place, although we will still need to see evidence of compliance with one or more of the quality system standards listed in Table 2. You must provide us with a certified copy of your domestic market license(s) in accordance with Table 1.

   Table 1 – Licensing requirements in the five GHTF founding member countries

	Australia [4]	Canada	European Union	Japan	United States
Marketing permit/ condition	GMPALS License or CE Mark	Device license	CE mark	Device license	510k device letter

   Table 2 - Acceptable quality system standards in the five GHTF founding member countries

Country	Quality system standards for medical devices	Certification body
Australia	ISO13485 or ISO13488	Government or third party accredited by the government
Canada	ISO13485 or ISO13488	Third party accredited by the government
European Union	ISO13485 or ISO13488	Notified Bodies
Japan	GMP (QS Standard for medical devices #1128)	Government
United States	QS (21 CFR part 820)	Government

2. **Option 2: No license in a GHTF founding member country:** If your device does not have Option 1 market clearance then your manufacturing process must meet one or more of the quality system standards listed in Table 2. You must provide us with documentary evidence of your conformity to these standards from a certification body accredited by the regulatory authorities in one of the GHTF founding member countries. The documentary evidence must take the form of certified copies of the relevant paperwork.

3.7 How do I apply for pre-qualification?

You should send an introductory letter, by airmail, surface mail or courier service, to the PQS Secretariat at WHO, Geneva, giving the following information:

[4] New, proposed legislation.

- describe the devices that you have to offer and give the relevant device category for each product – see 3.5;
- list the standards to which each device conforms and briefly describe the current licensing situation for each device;
- include 20 samples of each device from each manufacturing site for preliminary inspection purposes.
- On a voluntary and strictly confidential basis manufacturers are requested to provide brief details of the location and capacity of your manufacturing site(s) (both for products for which you are seeking pre-qualification and non-WHO products). WHO requests this information, as it does from vaccine producers, for the public health good. It is not a prerequisite for qualification.

There is no need to send a separate comprehensive dossier for each product at this stage – the PQS Secretariat will write to you listing the specific information that is required.

Envelopes or packages should be clearly marked: **PRELIMINARY PQS PRE-QUALIFICATION APPLICATION** and addressed to:

PQS Secretariat
Access to Technologies
Department of Immunization, Vaccines & Biologicals
World Health Organization
CH-1211
Geneva 27
Switzerland

Emailed and faxed applications may be acknowledged, but they will not be processed because we must have sight of the device samples before proceeding. We may contact you by telephone or email if we have specific queries.

Once we have received your introductory letter we will write to you to confirm which products are of interest to us and we will list the information that we require you to submit in order to make a formal application for pre-qualification – see Section 3.8. Alternatively, if it is evident from the information contained in your introductory letter that one or more of your devices is unsuitable, we will advise you accordingly.

3.8 How do I prepare a product dossier?

You must submit a separate and complete product dossier for each type of device that you have offered and which we have accepted as being suitable for evaluation. One dossier is required for each volume of syringe (for example, if you submit 1 ml, 2 ml and 5 ml syringes we will require three dossiers).

If you are offering a syringe that is manufactured at more than one manufacturing site we will require a separate dossier for each named site. Alternatively you may specify that the syringe will be supplied from one named manufacturing site only.

We will send you a letter listing the information that we require and we will enclose relevant background documents, including a further copy of this guideline. Each dossier you prepare must contain the following:

1. A covering letter.
2. A countersigned copy of the letter of invitation received from WHO, headed: **Application for pre-qualification of a single-use injection device under the PQS system: Pre-qualification information pack.** By countersigning this letter you confirm that you have read and agreed to abide by WHO's standard Terms and Conditions for pre-qualification.
3. The non-refundable Dossier Examination Fee; the amount requested will be the fee current at the date of application.
4. A completed *Product Summary Sheet Questionnaire* (see Annex 5.3) supported by the following material:
   - Confirmation that you are the Legal Manufacturer of the device.
   - General information about the manufacturer, including name and address.
   - Confirmation of the brand name of the device.
   - Product specifications, including details of product marking and traceability.
   - A manufacturer's certificate specifying the needle size and the needle length supplied with the device.
   - Details of the regulatory situation in the country of origin, including certified photocopies of the original assessment report issued by the relevant national regulatory authority.
   - Where applicable, details of the regulatory approval for the device in other countries, including certified photocopies of original documents.
   - Documentary evidence that the device conforms to the relevant ISO standard.
   - Full product license details, including certified photocopies of current license(s).
   - Certified photocopies of your current quality system certification issued by one of the certification bodies listed in Table 2.
   - Vigilance reports as reported to competent authorities (if any).
   - Other evaluation report(s) (if any).
5. A minimum of twenty samples of the injection device, in sealed unit containers, all taken from the same lot and packed within unopened secondary container(s).
6. Indicative cost of the product per unit, EXW, for 100,000 units, 1 million units and 10 million units. This information is requested on a voluntary basis and is not a prerequistite for qualification.

Packages should be clearly marked: **PQS PRE-QUALIFICATION APPLICATION** and addressed to:

PQS Secretariat
Access to Technologies
Department of Immunization, Vaccines & Biologicals
World Health Organization
CH-1211
Geneva 27
Switzerland

Reminder: Submit one dossier for each device. If the device is manufactured at more than one manufacturing site, you must submit one dossier for each site.

3.9 How much will I pay?

We will charge you on a cost recovery basis for the initial evaluation of your dossier. If your device is pre-qualified you will also be required to pay an annual re-evaluation fee as described in 3.11.2. The current fee scale, which will remain fixed until 31 December 2005, is shown in Table 3. (*WHO will review the fee scale at the end of 2005).*

Table 3 - Cost recovery fees to be paid to WHO (2005)

Step	**Fee to be paid to WHO**
Dossier examination fee	US$ 1,000
Annual re-evaluation fee	US$ 700

Note that these fees will be charged for each and every device you submit.

3.10 The dossier evaluation process

We will review the contents of your dossier. If anything is missing we will contact you in writing giving you a period of one month to provide the missing information, dossier fee or samples. If you fail to respond by the end of this period of grace we will return your dossier; the dossier examination fee will not be refunded. In addition we will not evaluate your dossier until the dossier fee has been paid in full.

Once we have a complete dossier and have cleared your Dossier Examination Fee, we will evaluate the information and samples you have supplied. We may appoint an independent evaluator to carry out this work. In order to avoid conflicts of interest and to protect your proprietary information, all our consultants will be required to sign a confidentiality agreement– see Annex 5.2, clause 11. If queries arise during the evaluation process, you may be contacted.

ISO-compliant devices: Devices that conform to one of the cited ISO standards do not need to be tested. Such devices can, in principle, be accepted on the basis of evidence supplied by the manufacturer that the device conforms to the relevant standards.

3.11 Evaluation results and the approval process

The PQS Secretariat will monitor the evaluation process and will endeavour to process applications as rapidly as resources allow; it will receive and review the evaluation results. The PQS Steering Group makes all final decisions on pre-qualification. WHO commit to a time limit of six weeks for the process from receipt of a complete dossier. The clock will stop if a dossier submission is incomplete, and not restart until the missing documents are received.

If the results of the evaluation are satisfactory we will write to tell you that your device has been pre-qualified for procurement by United Nations Agencies and that it will be listed on the PQS database. We will inform you if there are any remaining issues. We will expect you to deal with any outstanding issues before the next annual product review.

If the evaluation results are unsatisfactory you will be informed why the product is not suitable. Our decision is final and we will not enter into correspondence with unsuccessful candidates.

3.12 Maintaining pre-qualified status

The performance of your product and of your company will be kept under continual review through the formal PQS review procedure and throughout the procurement process at the various UN procurement agencies.

It is essential that you keep us fully informed about any significant change you make to the specifications of the product, to the manufacturing process or to the manufacturing site. If you do not do so, your device may loose its pre-qualified status – see section 3.12.

3.12.1 The extra-ordinary PQS review process

If serious problems arise with the product, leading to vigilance reporting, we reserve the right to re-evaluate your pre-qualification status at any time. A serious problem is an adverse event, device failure or other circumstance requiring immediate action. Generally, we will tell you about the problem and ask you to resolve it by an agreed date. However, if the problem is severe, we may suspend your pre-qualification status until it is resolved. Under some circumstances – for example bankruptcy or receivership – we will withdraw your pre-qualification status entirely.

3.12.2 The annual PQS review process

All PQS pre-qualified injection devices will be reviewed once a year at a single fixed time, that will be communicated to you at the time prequalification is granted, against a standard checklist based on Annex 4.3.

The annual review process will consider all relevant aspects of your device, including those referred to in Section 3.12. If we have previously highlighted problems which you need to resolve by an agreed date, you must keep us informed about your progress.

At least one month in advance, we will remind you of the date of the review and you must ensure that we receive the annual re-evaluation fee together with certified copies of all relevant time-expiring documentation and licensing arrangements by the time the validity of the previous documents has lapsed, in accordance with clause 8 of the Terms and Conditions set out in Annex 5.2. For example you must provide us with a certified copy of your annual product license renewal(s) before the previous one(s) expire(s) and you must submit a certified copy of the periodical renewal of your quality system certification issued by one of the certification bodies listed in Table 2. No period of grace will be allowed for the renewal of such documents and the presence of up-to-date documents in our files is a mandatory condition of pre-qualification. Note also that you are required to advise us whenever you receive an additional license from another GHTF founding member.

Envelopes or packages for the annual review should be clearly marked: **PQS ANNUAL RE-EVALUATION DOSSIER**, and addressed to:

PQS Secretariat
Access to Technologies
Department of Immunization, Vaccines & Biologicals
World Health Organization
CH-1211
Geneva 27
Switzerland

You should be aware that the first annual review may take place less than one year after your device is initially pre-qualified. This is because the review takes place on an annual basis at a single fixed time which may fall before a 12 month period has passed since your device was pre-qualified. You will still be required to pay the re-evaluation fee and to submit any necessary paperwork.

We will only inform you of the results of the annual review if we identify specific problems that require your attention. We will also inform you if your pre-qualification status is suspended or withdrawn as a result of the review.

3.13 Loosing pre-qualified status

There are several ways in which you could loose your status as a pre-qualified manufacturer. These include, but are not confined to, the following:

- if you change the manufacturing site with or without notifying us of your intention to do so (Annex 5.2, clause 8);
- if you change the manufacturing process in an unacceptable way (one that negatively effects the performance of the device) with or without notifying us of your intention to do so (as defined in Annex 5.2, clause 8);
- if you change the device specification in an unacceptable way (Annex 5.2, clause 8);
- if we receive reports from the UN procurement agencies showing that your production quality control is poor or inconsistent (Annex 5.2, clause 8);
- if you fail to notify us concerning device failures or adverse events or if you fail to collaborate with the complaint monitoring procedure for single-use injection devices (Annex 5.2, clauses 8 and 10);
- if the functioning of the device in the field is shown not to be meeting the performance requirements;
- if you fail to provide evidence of annual license renewal(s) for the device or any other relevant time expiring documentation(Annex 5.2, clause 8);
- if you go into bankruptcy or receivership.

4.0 Checklists

This section provides you with three checklists designed to ensure that you send us all the information that we require at each of the stages specified.

4.1 Preliminary application checklist

Refer to Section 3.7 - Have you included the following?	
1. A covering letter.	☐
2. A description of each device that you wish to offer for evaluation.	☐
3. Brief details of each of your manufacturing sites.	☐
4. Confirmation of the production capacity of each of your manufacturing sites.	☐
5. A list of the standards to which each device conforms.	☐
6. A brief description of the licensing situation for each device.	☐
7. Twenty clearly labelled samples of each device. If the device is made at more than one site, provide samples from each manufacturing site.	☐
8. A correctly labelled and addressed package.	☐

Reminder: Your preliminary application can include information about more than one device and more than one manufacturing site.

4.2 Dossier submission checklist

Refer to Section 3.8 - Have you included the following items for each device and for each manufacturing site?	
1. A covering letter.	☐
2. A countersigned copy of the letter of invitation received from WHO	☐
3. The correct Dossier Examination Fee, in US dollars.	☐
4. Completed *Product Summary Sheet Questionnaire* supported by the following material:	☐
• Confirmation that you are the Legal Manufacturer of the device.	☐
• General information about the manufacturer, including name and address.	☐
• Confirmation of the brand name of the device.	☐
• Product specifications, including details of product marking and traceability.	☐
• A manufacturer's certificate specifying the needle size and the needle length supplied with the device.	☐
• Certified photocopy of the regulatory approval for the device in the country of origin issued by the relevant national regulatory authority.	☐
• Where applicable, details of the regulatory approval for the device in other countries, including certified photocopies of original documents.	☐
• (ISO-compliant devices only): Documentary evidence that the device conforms to the relevant ISO standard.	☐
• Full product license details, including certified photocopies of current license(s).	☐
• Certified photocopies of your current quality system certification issued by one of the certification bodies listed in Table 2.	☐
• Post-market surveillance report(s) (if any).	☐
• Other evaluation report(s) (if any).	☐
5. A minimum of twenty samples of the injection device, in sealed unit containers, all taken from the same lot and packed within unopened secondary container(s).	☐
6. Indicative cost of the product per unit, EXW, for 100,000 units, 1 million units and 10 million units.	☐
7. A correctly labelled and addressed package.	☐

Reminder: You must submit one dossier for each device. If the device is manufactured at more than one manufacturing site, you must submit one dossier for each site.

4.3 Annual review checklist

Refer to Section 3.12.2 - Have you included the following items for each pre-qualified device and for each manufacturing site?	
1. A covering letter specifying the device to which the dossier refers.	☐
2. The annual re-evaluation fee in US dollars.	☐
3. Certified photocopy of your annual license renewal(s) if the current license(s) is/are due to expire before the review meeting.	☐
4. Certified photocopy of any additional license(s) that have been issued by a GHTF founding member since you made your last submission.	☐
5. Certified photocopies of all other time-expiring documentation that you have renewed since you made your last submission, including renewal of your quality system certification issued by one of the Certification Bodies listed in Table 2.	☐
6. Details of changes to the manufacturing site since you made your last submission.	☐
7. Details of changes to the manufacturing process since you made your last submission.	☐
8. Details of changes to the product since you made your last submission.	☐
9. Details of all adverse events reported to you during the past year.	☐
10. Details of all device failures reported to you during the past year.	☐
11. Progress report on the resolution of any problems reported to you by the PQS Secretariat.	☐
12. A list of other matters that you wish to draw to our attention.	☐
13. A correctly labelled and addressed envelope/package.	☐

Reminder: You must submit one dossier for each device. If the device is manufactured at more than one manufacturing site, you must submit one dossier for each site.

5.0 Annexes

Annex 5.1 - Definitions

The following definitions apply to this document:

Adverse event	An incident resulting in permanent impairment, hospitalization, congenital malformation, injury or death to patients or users of a single-use injection device.
Certification Body	A *Certification Body* is a government department or agency or a third party organization that provides services for conformity assessment following completion of an independent assessment verification and qualification process. In this document the term is taken to include *Notified Body.*
Certified copy	Wherever a *certified copy* or *certified photocopy* is requested, the copy must be certified as a true copy of the original document by a person registered to practice law in the *Legal Manufacturer's* country of origin and must be endorsed with the legal practitioner's official stamp and signature.
Correspondence	Includes mail, fax and email.
Device	An invention serving a particular purpose.
Device failure	The failure of a single-use injection device to meet the specifications issued by the manufacturer.
Evaluator	An individual or organization (including a WHO-accredited testing laboratory) responsible for evaluating or assessing any aspect of a product as described in this document.
in writing	Where the phrase *in writing* is used this means correspondence must be transmitted by mail, fax or email.
Notified Body	A *Notified Body* is a third party organization that has been appointed to provide services for conformity assessment following completion of an independent assessment verification and qualification process[5] - see also *Certification Body*.
Manufacturer	In the context of this document the word *manufacturer* means the *Legal Manufacturer.*

[5] Definition derived from EU *New Approach*.

Legal Manufacturer	*Legal Manufacturer* means the natural or legal person with responsibility for the design, manufacture, packaging and labelling of a product or device before it is placed on the market under his own name, regardless of whether these operations are carried out by that person himself or on his behalf by a third party[6].
Period of grace	Period allowed after the expiry of a license or other time-expiring document and before the renewed license or document is presented.
Primary container[7]	The *primary container* comprises a single self-contained syringe unit housed within a sterile *unit container.*
Product	In this document, where the word product is used on its own, it includes *device.*
QA	Quality Assurance.
Secondary container[4]	The *secondary container* is the packaging which contains more than one *unit containers.*
Storage container[4]	The *storage container* is a carton or other form of packaging containing a specific number of *secondary containers.*
Unit container[4]	The *unit container* is the sterile enclosure which encloses a single self-contained syringe unit.
Verification	A verification protocol describes in detail how the performance of a *product* or *device* will be tested or otherwise evaluated as part of the PQS product pre-qualification procedure.

[6] Definition derived from Article 1 2.(f) of the EU Medical Device Directives.

[7] Definition derived from draft ISO DIS 7886-3

Annex 5.2 – Standard Terms and Conditions

The Terms and Conditions and Definitions set out below will apply to all manufacturers of PQS pre-qualified injection devices. You should familiarize yourself with this document and ensure that you comply fully with the on-going reporting requirements set out therein. Failure to do so may result in the suspension or withdrawal of your pre-qualification status.

TERMS AND CONDITIONS FOR THE PRE-QUALIFICATION OF SINGLE-USE INJECTION DEVICES

1. ***Examination of dossier:*** The Product Dossier will be screened by WHO for completeness prior to the evaluation of the dossier. The dossier can be rejected on grounds of incompleteness and returned to the manufacturer. Complete dossiers will be retained for evaluation purposes.
2. ***Dossier Examination Fee:*** The Dossier Examination Fee is non-refundable and must be paid in full, in the specified currency, before the dossier can be formally examined by WHO.
3. ***Evaluation:*** The WHO unit responsible for the evaluation will be independent from all UN agency procurement units. Every single-use injection device will be evaluated against the relevant PQS performance specification and product verification protocol, current at the time of the evaluation. The manufacturer will receive a letter from WHO advising on the outcome of the evaluation process with regard to the specific product(s) of that particular manufacturer.
4. ***Meaning of pre-qualification:*** The granting of pre-qualification status following the evaluation process indicates that the single-use injection device is technically satisfactory for procurement by United Nations Agencies for the purpose for which the device is intended, subject to any limitations set out in the PQS website or catalogue.
   However, the granting of pre-qualification status does not guarantee that an acceptable commercial arrangement can be reached between the supplier of the single-use injection device and the purchaser;. In this context the word, 'purchaser', could cover more than one of the UN agency procurement units, including UNICEF, IAPSO, UNFPA, and WHO.
5. ***Publication:*** Following satisfactory evaluation, the single-use injection device, as manufactured at the specified manufacturing site, will be included in the list of 'pre-qualified' PQS products and WHO will inform the interested UN agency procurement unit(s) accordingly. Details of the product will then be posted on the PQS website and may also be published in a hard copy catalogue
6. ***Re-evaluation:*** The product will be subjected to review once a year, unless major changes occur in the meantime. Manufacturers are required to ensure that all relevant time-expiring licenses and certificates remain valid and must provide WHO with evidence of the periodic renewal of such documents in the form of certified copies. Manufacturers must advise WHO in writing of any changes that may have an impact on the safety, performance, efficacy or quality of the product. Manufacturers must also advise WHO in writing of any contemplated changes to the product, to the manufacturing process or to the manufacturing site. If there is a change in manufacturing site WHO will require the manufacturer to make a new pre-qualification submission.

   Re-evaluation may also be carried out in the following situations:
   - If any omission by the manufacturer in the initial evaluation procedure, or during the follow-up activities, is evident in relation to the requirements, including compliance with quality system standards and failure to notify complaints. If any batch or batches of supplied product(s) are documented by WHO, or one or more of the UN agencies or organizations, not to be in compliance with the agreed specifications of the product or to reveal failure(s) regarding safety, performance or quality of the device;
   - If the investigation of a complaint considered leads to the conclusion that the quality and/or safety of the product is in question.
7. ***Monitoring of complaints:*** The manufacturer of a pre-qualified single-use injection device must agree to collaborate with WHO and, where relevant with other UN agencies, in the investigation of complaints regarding device failure and adverse events relating to the device. Upon receipt of a complaint the responsible manufacturer will investigate the reported complaint, in collaboration with WHO or other relevant UN agencies. WHO will maintain a database of complaints ./...

	Following the investigation, the manufacturer will report to the WHO. The WHO will provide UN agencies with the manufacturers written report of the problem and with recommendations for action, if any. WHO reserves the right If circumstances justify it (vigilance reporting), to report the complaint to the national regulatory authority where the device was used and/or to the national regulatory authority where the manufacturers notified body is located.
8.	***Confidentiality undertaking:*** WHO will treat, and will require evaluators of product dossiers to treat all information to which they will gain access during the evaluation, or otherwise in connection with the discharge of their responsibilities in regard to the pre-qualification of PQS products as confidential. In addition, the evaluators of product dossiers will be required to sign a Declaration of Interest. If based on this Declaration of Interest, it is felt that there is no risk of real or perceived conflict of interest and it is thus deemed appropriate for evaluators to undertake this work, they will discharge their functions exclusively as advisers to WHO. A sample of the confidentiality and declaration of interest undertaking for evaluators of product dossiers can be obtained on request.
9.	**The following disclaimer applies to all products that are accepted for inclusion on the PQS database.** *Disclaimer:* Inclusion in the PQS database does not constitute an endorsement, or warranty of fitness, of any product for a particular purpose, including in regard to its safe and appropriate use in immunization programmes. WHO does not furthermore warrant or represent that: 1) the database is complete or error free and/or that 2) the products that have been found to meet the standards recommended by WHO, will continue to do so and/or that 3) the products listed have obtained regulatory approval for use in every country of the world or that its use is otherwise in accordance with the national laws and regulations of any country, including but not limited to patent laws. In addition, WHO wishes to alert procuring UN agencies that the improper storage, handling and transportation of products may affect their quality, efficacy and safety. WHO disclaims any and all liability and responsibility for any injury, death, loss, damage or other prejudice of any kind whatsoever that may arise as a result of, or in connection with the procurement, distribution and use of products included in the list.
DEFINITIONS:	
1.	*Adverse event* means an incident resulting in permanent impairment, hospitalization, congenital malformation, injury or death to patients or users of a single-use injection device.
2.	Wherever a c*ertified photocopy* is requested, the photocopy must be certified as a true copy of the original document by a person registered to practice law in the *Legal Manufacturer's* country of origin and must be endorsed with the legal practitioner's official stamp and signature.
3.	*Device failure* means the failure of a single-use injection device to meet or exceed the specifications issued by the manufacturer.
4.	In the context of these terms and conditions the word *manufacturer* means the *Legal Manufacturer*.
5.	*Legal Manufacturer* means the natural or legal person with responsibility for the design, manufacture, packaging and labelling of a product or device before it is placed on the market under his own name, regardless of whether these operations are carried out by that person himself or on his behalf by a third party.
6.	The *primary container* comprises a single self-contained syringe unit housed within a sterile unit container.
7.	In the context of these terms and conditions, where the word *product* is used on its own, it means *single-use injection device*.
8.	The *secondary container* is the packaging which contains more than one *unit containers*.
9.	*Single-use injection device* includes single-use syringes used in conjunction with single-use needles, auto-disable (AD) syringes designed specifically for immunization and syringes with a reuse-prevention feature for therapeutic purposes.
10.	The *storage container* is a carton or other form of packaging containing a specific number of *secondary containers*.
11.	The *unit container* is the sterile enclosure which encloses a single self-contained syringe unit.

Annex 5.3 – Product Summary Sheet Questionnaire and instructions

		Information item	INJECTION DEVICE PRODUCT SUMMARY SHEET (Complete one questionnaire per product and per manufacturing site – see note 1)				
1	☐	**Device description**					
2	☐	Brand name				**Remarks**	
3	☐	Vendor status	☐ Manufacturer ☐ Wholesaler ☐ Distributor ☐ Other (specify)				
			Name	**Address**	**Phone and Fax**	**Contact person for quality assurance**	**Web-site, e-mail**
4	☐	Vendor					
5	☐	Manufacturer					
	☐	Manufacturing Site					
6	☐	Parent company (if any)					

			Regulatory authority (check all applicable)	**Number**	**Device name as submitted to authorities**
7	☐	Compliance with regulations	❑ Australia	License number:	
			❑ Canada	License number:	
			❑ European Union	CE mark number:	
			❑ Japan	License number:	
			❑ United States	510(k) number:	
			❑ Other (specify):		

			Standards used (check applicable)	**Certification body.** Specify name & country & attach copy of the certificate. (See note 2)	**Last audit date**	**Expiration date**
8	☐	Conformity with quality system standards	❑ ISO13485 or ISO13488			
			❑ Japan QS Standard #1128			
			❑ United States QS (21 CFR part 820)			
			❑ Other (specify, e.g. ISO9001:2000)			

			Standards used (check applicable)		
9	☐	Conformity with product standards	❑ ISO 7864 for needles		
			❑ ISO 7886-3 for AD syringes for immunization:		
			❑ ISO 7886-4 for syringes with a reuse prevention feature		
			❑ ISO 8537 for syringes for insulin injection		
			❑		
			❑		
			❑		
10	☐	Post-market surveillance reports	❑		
11	☐	Other evaluation reports	❑		

Notes: 1) An electronic version of this questionnaire may be downloaded from http://www.who.int/vaccines-access/vacman/pis/new%20sheets%20intro.htm. 2) For example: Notified bodies in the European Union; Quality Systems Registrars in North America.
3) Product testing must include sterility, packaging and labelling requirements.

Instructions for completing the Product Summary Sheet Questionnaire

General note: All applicants must complete items 1, 2, 3, 4, 5, 6, 8, 9, 10 and 11. Complete item 7 *only* if the device has a license/clearance in one of the GHTF founding member countries.

Item 1: Give a brief description of the device.

Item 2: Give the brand name that is used on the market. If more than one name is used, please list all names.

Item 3: Check the appropriate box to indicate the status of the Vendor.

Item 4 and item 5: In some cases the vendor may also be the manufacturer. In such cases, provide all the requested information under both headings, even if the details are identical.

Item 6: If the manufacturer is a subsidiary of a parent company, or is under contract to another company, please supply the necessary information. Traceability of the device to the Legal Manufacturer must be clearly stated on all packaging. The Legal Manufacturer's documentation system must also include traceability of the device to the original manufacturing site.

Item 7: Check each GHTF founding member country in which the regulatory authority has licensed/cleared the device. In each case, give the license or clearance number and state the device name that was submitted to the authority. Note that the submitted device name may be different from the brand name; we require this information so that we can verify your market clearance with each of the regulatory authorities.

Item 8: Check all quality system standards applicable to the manufacturing site. Against each checked standard state the name and country of origin of the Certification Body which verified compliance with the standard and provide a certified copy of the quality system certification. State the date of the last certification audit and the date of expiry. The maximum period between audits must not exceed three years.

Item 9: Check all product standards applicable to the device. Against each of the checked standards state the name of the test laboratory which carried out the test and state the name of the body which accredited the laboratory. Product testing must include sterility, packaging and labelling requirements. We require a copy of the internal test certificate (ISO-compliant devices)

Item 10: Provide all post-market surveillance reports issued by regulatory authorities, users or other parties and state the source of each.

Item 11: If available, provide any other third party evaluation report

6.0 References

ISO standards and WHO performance specifications:

1. ISO 7864:1993 *Sterile hypodermic needles for single use.*
2. ISO 7886-1:1993 *Sterile hypodermic syringes for single use - Part 1: Syringes for manual use.*
3. ISO 8537:1991 *Sterile single-use syringes, with or without needle, for insulin.*
4. ISO 7886-3: *Sterile hypodermic syringes for single use – Part 3: Auto-disable syringes for fixed dose immunization*
5. ISO DIS 7886-4: *Sterile hypodermic syringes for single use – Part 4: Syringes with reuse prevention feature* (draft standard, in preparation).

Other references:

1. *WHO. A guide for the quality assurance of single-use injection equipment. WHO/BCT/03.02.*
2. WHO. *Best infection control practices for intradermal, subcutaneous and intramuscular needle injections.* WHO/BCT/DCT/01.02.
3. *WHO. Bundling principles.* WHO/V&B/99.25.
4. WHO. *From PIS to PQS: A new system for specifying, testing and pre-qualifying products for use in immunization programmes.* Proceedings of 2004 TechNet consultation in Antalya, Turkey: http://www.who.int/vaccines-access/vacman/pis/pqs.htm
5. WHO. *Guiding principles to ensure injection device security.* WHO/BCT/03.12.
6. WHO. *Medical device regulations, global overview and guiding principles.* Geneva: World Health Organization, 2003. ISBN92 4 154618 2
7. WHO. *Procedure for assessing the acceptability, in principle, of single-use injection devices for procurement by United Nations agencies.* WHO/BCT/03.09.
8. WHO/UNICEF *Product Information Sheets - 12th Edition 2000*. WHO/V&B/00.13.
9. Temporary PQS link: http://www.int/vaccineaccess/vacman/pis/new%20sheets%20intro.htm

REVISION HISTORY FORM

(Form number: FCH/IVB /ATT/GEN/F002)

SOP Number

Date of original version:

REVISIONS

Date	Reason	Authorized by (Signature and Name)