Introduction to PQS

Specifying, testing and pre-qualifying products for use in immunization programmes

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Disclaimer
Where specific products or services are mentioned in this document this is for
illustrative purposes only. WHO does not intend to imply any preference for these
products or services.
**Acronyms**

ANSI    American National Standards Institute  
CEN    Conseil Européen pour la Normalisation  
EHT    Essential Health Technologies  
ISO    International Standards Organization  
IVB    Immunization, Vaccines and Biologicals (Department of)  
MSF    Médecins Sans Frontières  
PATH    Program for Appropriate Technology in Health  
PQS    Performance, Quality and Safety  
QAC    Quality Assurance Centre  
QSS    Quality, Safety and Standards  
SAGE    Strategic Advisory Group of Experts  
SIGN    Safe Injection Global Network  
SOP    Standard Operating Procedure  
TLAC    Technologies and Logistics Advisory Committee  
TSC    Technical Steering Committee  
UNICEF-SD    United Nations Children’s Fund – Supply Division  
VP    Verification Protocol  
WHO    World Health Organization
1. Introduction

Since the early days of EPI in the late 1970’s there has been a need for specialised cold chain equipment designed to meet the demanding performance requirements of the developing world, where fuel supplies and electrical power are limited and unreliable and climatic conditions are often challenging.

In order to meet this need, WHO, in consultation with UNICEF Supply Division, drew up performance specifications and test procedures and collaborated with a small number of manufacturers and testing laboratories to develop a range of key products for the vaccine cold chain. Products that successfully passed the testing stage were listed in the WHO/UNICEF Product Information Sheets (PIS), the last paper edition of which was published in the year 20001.

Over the years, the scope of the PIS was extended. Auto-disable syringes and low-cost waste management products have been introduced to help ensure that immunization injections are safe and that used injection equipment can be properly disposed of. Vaccine Vial Monitors (VVMs) have been developed so that the temperature exposure of individual vaccine vials can be monitored.

After an extended overlap period, PIS has now been replaced by the PQS (Performance, Quality and Safety) system. The new system is designed to bring in a wider range of manufacturers, to introduce further new technologies and to meet the challenges posed by the introduction of a growing range of new and more expensive vaccines.

The PIS document was a combination of product catalogue and buyer’s guide. PQS will perform the same functions, but information will be in electronic format so that it remains up-to-date. This document describes the scope of the system, how it is organised, how specification documents are written and amended, and how products are pre-qualified; it covers the annual review process, accreditation of test laboratories and outlines the content of the PQS website.

2. The scope of PQS

PQS is a process for pre-qualifying products and devices so that member states and UN purchasing agencies are assured of their suitability for use in immunization programmes. It addresses the responsibilities and needs of four key players.

- **WHO** is the professional UN agency responsible for giving advice on immunization-related issues. Part of this advisory role is to characterise the products that are needed to meet known operational requirements and field conditions.

- **UN procurement agencies** need to know that the products they purchase on behalf of client countries are fit for purpose.

- **Client countries** need to know the performance characteristics of the products they are ordering, and how and where they should be used.

- **Industry** needs a fair basis for tendering existing products and for investing in development and innovation to meet future needs.

PQS is open and transparent and all relevant documents and procedures will be published on the PQS website; the intention is to encourage a wide range of

1 Newer PIS products are listed on the WHO website.
manufacturers to apply for pre-qualification so that a competitive marketplace develops. User feedback on the performance of individual products will actively be sought and PQS will establish mechanisms for obtaining data on field performance in a systematic manner.

The process starts with the identification of a product need. A market investigation establishes whether suitable products already exist, or whether further product development or innovation is required. During this process key manufacturers are identified. In consultation with independent and industry-based technical specialists, performance specifications and verification protocols are drawn up. Once these documents have been approved and published, manufacturers are invited to submit products for pre-qualification.

Products that pass the verification process are then listed on the PQS website. Every 12 months there is an annual review of all pre-qualified products; the review team check whether there have been significant defects or failures associated with a product, if the design or manufacturing process has changed, and whether certification documentation is up-to-date. Problem-free products are then re-validated for a further 12 months. If problems are identified, the manufacturer is formally notified. If the subsequent response is unsatisfactorily, the product’s pre-qualification status may be suspended or lost.

Figure 1 shows the product categories currently listed for PQS pre-qualification and indicates the type of documentation against which application for pre-qualification are assessed. In the case of the transport category no standards are set, but the PQS website includes a buyer’s guide. This covers motorcycles, general purpose vehicles and refrigerated vehicles.

**Figure 1 – PQS product categories**

<table>
<thead>
<tr>
<th>PQS cat.</th>
<th>Description</th>
<th>Buyer’s guide</th>
<th>ISO standard</th>
<th>PQS spec &amp; VP</th>
</tr>
</thead>
<tbody>
<tr>
<td>PQS - E01</td>
<td>Freezer rooms and cold rooms</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PQS - E02</td>
<td>Transport</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PQS - E03</td>
<td>Refrigerators and freezers, including PV</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PQS - E04</td>
<td>Cold boxes and vaccine carriers.</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PQS - E05</td>
<td>Icepacks</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PQS - E06</td>
<td>Temperature monitoring devices.</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PQS - E07</td>
<td>Cold chain accessories.**</td>
<td>To follow</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PQS - E08</td>
<td>Single use injection devices.</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PQS - E09</td>
<td>Steam sterilizers</td>
<td>Old PIS category, now withdrawn</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PQS - E10</td>
<td>Safety boxes &amp; needle cutters</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PQS - E11</td>
<td>Specimen collection equipment **.</td>
<td>To follow</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PQS - E12</td>
<td>Spare category</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PQS - E13</td>
<td>Therapeutic injection devices.</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

** Category not yet activated
Procedures are also in place so that a product category can be withdrawn in response to a specific policy change or when a need disappears as a consequence of technical or operational developments.

3. How PQS is organised

Figure 2 shows the organizational structure of PQS. The core of the system is a permanent secretariat based at WHO Geneva. Located within the Quality, Safety and Standards section of the Department of Immunization, Vaccines and Biologicals (IVB/QSS), this secretariat is responsible for the day-to-day operation of the PQS system and the development and continuing maintenance of approved documents. These include standard operating procedures, specifications and verification protocols and PQS guidance documents.

The PQS Secretariat (Secretariat): In addition to working with the relevant departments within WHO and UNICEF-SD, the Secretariat’s main tasks is to establish and maintain the PQS website and database, to liaise with the PQS Steering Group and the ad-hoc specification and field monitoring working groups, and external consultees, to commission and supervise contract work carried out by technical specialists and testing laboratories, to manage and co-ordinate the product pre-qualification process, to co-ordinate product feedback reports and to review and disseminate the results of field monitoring activities.

A past example is the removal of reusable syringes and steam sterilisers in response to the WHO-UNICEF-UNFPA Joint statement on the use of auto-disable syringes in immunization services. WHO/V&B/99.25.
The PQS Steering Group (PQS-SG): The PQS-SG provides strategic guidance and oversight of the PQS process. Core membership of the PQS-SG comprises one person from each of the relevant departments within WHO and UNICEF-SD. In consultation with bodies such as TLAC and SAGE, the Steering Group monitors ongoing developments in the immunization programme and directs the Secretariat to take appropriate action. In addition it:

- monitors and guide the work of the specialist working groups;
- oversees the peer-review process that is used to monitor the quality and consistency of the PQS specifications and verification protocols;
- carries out technical reviews of existing PQS performance specifications and product verification protocols;
- directs the addition or omission of PQS product categories;
- directs the writing of new or revised performance specifications and product verification protocols;
- directs the withdrawal of these documents when they become out-dated.

Specification Working Groups (SWG): The principal responsibility of the SWGs is to develop new performance specifications and product verification protocols and to highlight the need for revisions to existing documents. Once the need for a new performance specification is established, the relevant SWG draws up basic design criteria; this document is used to guide discussions with the technical specialist who is appointed to prepare the detailed specification and any associated product verification protocol. In addition group members consult with the Field Monitoring Working Group.

Field Monitoring Working Group (FMWG): Field monitoring is one of the key components of the PQS system. This process ‘closes the loop’ by ensuring that the performance of products in the field is systematically monitored and that feedback is sent to manufacturers so that their products can be improved. The FMWG is responsible for obtaining user feedback by liaising with Ministries of Health and other users of PQS products. In consultation with the Specification Working Groups the FMWG is also responsible for developing field monitoring methods to suit specific performance specifications.

Technical specialists, acting under the direction of the Secretariat, bring the necessary specialized skills to the task of writing and revising performance specifications, product verification protocols and other documents. In the course of their work these specialists consult closely with the relevant SWG and/or with the FMWG. Some of these individuals are WHO or UNICEF employees, some are independent consultants.

Together, these five entities have access to expertise from a range of external advisors, who are called on as required. These advisors include the following:

- Specialist agencies such as PATH, MSF, SCF.
- Testing laboratories.
- Standards bodies such as ISO\(^3\), CEN, ANSI, etc.
- Industry representatives. These may be experts offered by individual companies or appointees from the relevant industry trade associations.
- The TechNet21 and SIGN e-forums provide an essential pool of expertise from which to draw members of the ad-hoc working groups. These forums also

\(^3\) ISO worked closely with WHO-EHT on the development of the ISO standards for auto-disable syringes.
provide a convenient way to circulate draft documents for expert comment and peer-review.

- Ministries of Health and other users, whose roles in facilitating effective field monitoring are critical to the success of PQS.

4. **Standard operating procedures**

The PQS process divides into six major tasks: writing and revising performance specifications; writing and revising product verification protocols; pre-qualifying testing laboratories; pre-qualifying and re-evaluating products; field testing these products and, finally, obtaining feedback from users.

Standard operating procedures (SOPs) are in place to ensure that all these tasks are carried out in a consistent and systematic manner – see Figure 3. The figure shows the relationship between the internal procedures described in the SOPs and key external standards and processes which impact upon these procedures. For example, ISO/IEC 17025 and its related laboratory accreditation process is a pre-requisite for the pre-qualification of a PQS testing laboratory; accordingly this standard must be well understood by those who inspect and pre-qualify such organizations.

**Figure 3 – PQS standard operating procedures**

5. **Specifications and verification protocols and procedures**

Performance specifications and verification protocols and procedures are at the heart of the PQS process.

5.1 **Performance specifications**

A *performance specification* defines the functional requirements of a product and describes the environment within which it must operate. It must describe in a comprehensive, unambiguous and neutral way how these requirements are to be met so that it does not implicitly or explicitly favour products from any one manufacturer, country or geographical region. Wherever possible the specification
should refer to ISO or other published standards. Finally, it must comply fully with WHO immunization policies and guidelines current at the time of publication.

Industry can meet these performance specifications in two ways. Under the non-developmental route a manufacturer offers compliant items from an existing product range. Under the developmental route, selected manufacturers are identified and encouraged to modify an existing product or to develop a new one. A performance specification which targets commercially available products is likely to attract the widest and most economically competitive range of compliant products or devices. The developmental approach is adopted only after market investigation has established that no existing products meet the design criteria, and that the design criteria themselves cannot be further modified. Figure 4 describes the two routes.

**Figure 4 – Developing a performance specification**
5.2 Verification protocols and procedures

Every new product must be inspected or tested before it can be added to the list of pre-qualified products in the PQS database. The general term adopted for this process is verification. A verification protocol establishes whether a specific product from a specific manufacturer satisfies the requirements of the relevant PQS performance specification. There are four ways in which this is done:

1. **Verified compliance**: A product manufactured to meet a specific international standard or standards is verified by checking systematically that the manufacturing process is fully compliant.

2. **Type-examination**: Sample inspection is carried out against a checklist in a PQS-accredited test laboratory, or by an independent expert. Used for items that are not programme-critical.

3. **Independent type-testing**: Sample inspection and testing is carried out in a PQS-accredited test laboratory. Used for products that are programme-critical.

4. **Full Quality Assurance**: Site inspection by an independent inspector is carried out against a pre-defined checklist. Used for complex programme-critical products involving site-specific design and on-site installation work.

**Verified compliance**: Products, such as syringes and other medical devices are manufactured to meet a specific international standard. The producers of such products have to meet tough quality control standards throughout the manufacturing process, with these standards regularly monitored by external certification bodies and national regulatory authorities. Provided these certifications and approvals are in place and are maintained, such products can be pre-qualified on this basis alone – independent testing is not needed.

**Type-examination** involves the systematic inspection of product samples supplied by the applicant manufacturer. The technique is checklist-based and is a suitable verification method for items that are supplied in relatively small quantities. Where the risks arising from product failure are low it may also be an acceptable method for verifying high volume items. Finally the type examination route can be followed where quality control standards in the relevant industry are uniformly high. Under PQS, type examination will generally be delegated to an accredited test laboratory or to an independent specialist. Alternatively a type examination certificate issued by a reputable independent body may be an acceptable substitute.

**Independent type-testing** involves the physical testing of a number of product samples against a rigorously defined test protocol. This route is justified for complex high value products and also for simple high volume products where the risks arising from product failure are high – vaccine refrigerator thermometers are an example. Independent type testing will always be carried out by a PQS-accredited test laboratory.

**Full Quality Assurance** is applicable to complex high value, low volume products which require an element of site-specific design as well as on-site assembly and commissioning work; cold rooms and standby generator installations are examples which fall into this category. Manufacturers and/or approved installers offering such products cannot be pre-qualified solely on the basis of type-examination or type-testing because every instance of the product will in some way be unique. Instead pre-qualification must be based on a thorough assessment of technical specifications and quality control procedures, supported by references from other customers. To achieve full quality assurance, the manufacturer/installer should generally be ISO

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4 Currently this approach only applies to cold rooms and freezer rooms.
9001 accredited; in most cases the completed installation will also be inspected and approved by an independent inspector.

Figure 5 gives an overview of the procedure for deciding which of the four verification routes is suitable for a particular product.

**Figure 5 – PQS product verification routes**

6. **Pre-qualification and re-evaluation**

Before a product or device can be added to the PQS database, it must be formally pre-qualified. A product can only be pre-qualified if it complies with an international standard or a PQS performance specification and has been assessed against the relevant PQS product verification protocol.

Pre-qualification involves a linked sequence of activities. The manufacturer of a potentially suitable product is sent a *pre-qualification information pack* containing the relevant PQS performance specification and product verification protocol, WHO’s terms and conditions and other related material. The manufacturer then submits a *product dossier*. The dossier is checked by the Secretariat; if it is satisfactory the manufacturer is asked to send samples for formal verification in accordance with the applicable verification protocol. Only after this stage has been completed satisfactorily can the product be pre-qualified. Figure 6 outlines the procedure.
The Secretariat maintains a register recording details of all applications for product pre-qualification and another register of pre-qualified products. Once a product has been satisfactorily verified and approved, a datasheet is prepared and uploaded to the PQS website.

Once every twelve months, there is an annual review meeting. Manufacturers of products which follow the verified compliance route must submit a dossier containing certified copies of their current certifications and approvals as well as adverse event reports and other relevant documentary evidence. If the documentation is satisfactory, the product is re-validated for a further 12 months.

Other products are assessed and re-validated on the basis of a more general review which takes account of UNICEF-SD QAC reports, performance reports from the field and manufacturer’s change notifications and product defect reports, etc. Occasionally circumstances may also arise that require an emergency re-evaluation – for example if there are reports of serious product failure.

The Secretariat, in consultation with the PQS-SG can also suspend or remove a product from the PQS database if circumstances warrant these actions.
7. **Laboratory accreditation**

PQS includes procedures for accrediting test laboratories that comply with the ISO/IEC 17025 standard\(^5\). Test laboratories are used whenever a product is submitted for testing or type-examination against a PQS verification protocol. Some laboratories are also able to carry out full quality assurance inspections.

Each of these laboratories has a datasheet on the PQS database which specifies the product categories and types of verification have been accredited – see Figure 7.

**Figure 7 – Laboratory datasheet**

<table>
<thead>
<tr>
<th>PQS cat</th>
<th>Equipment type</th>
<th>Type-examination</th>
<th>Type-testing</th>
<th>QA inspection</th>
<th>The following equipment types are excluded</th>
</tr>
</thead>
<tbody>
<tr>
<td>E91</td>
<td>Cold rooms, freezer rooms</td>
<td>✓</td>
<td>n/a</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Standby generators</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Large voltage regulators</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E35</td>
<td>Refrigerators and freezers</td>
<td>✓</td>
<td>✓</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>E34</td>
<td>Solar systems</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>E36</td>
<td>Insulated containers</td>
<td>✓</td>
<td>✓</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>E37</td>
<td>Icepaks, cold water parks</td>
<td>✓</td>
<td>✓</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>E36</td>
<td>Temperature monitoring</td>
<td>✓</td>
<td>✓</td>
<td>IM05 - VVMs</td>
<td></td>
</tr>
<tr>
<td>E1</td>
<td>Cold chain accessories</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Small voltage regulators</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E98</td>
<td>Single-use injection devices</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E90</td>
<td>Safety boxes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E10</td>
<td>Needle destroyers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E11</td>
<td>Syringes malters</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E12</td>
<td>Inspectors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E11</td>
<td>Specimen collection</td>
<td>✓</td>
<td>✓</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>E13</td>
<td>Therapeutic injection centres</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**
1) Check shipping instructions with the laboratory to avoid problems with customs and to ensure safe delivery of test samples.

**Accreditation details**

ISO/IEC 17025 accreditation by: COFRAC  
Next reassessment date: 1 November 2008

Laboratories are included in the annual review process described above. The review meeting checks performance and compliance against a standard checklist – for example to establish that ISO 17025 accreditation is up-to-date.

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8. The PQS website

PQS product datasheets and related documents are currently published on a temporary PQS website. This site will be replaced later in 2009 by a fully developed interactive website which will provide a searchable resource allowing users to compare different products in each category, to download an up-to-date PDF product catalogue and to access related specifications and guidance documents.