HIGH-VOLTAGE TECHNOLOGY FOR AREAS WHERE EVEN THE BEST CAMERAS CAN SEE NOTHING, E. G. FOR LEAKAGE TESTING.

THE EVALUATION

Different tests with different sets of good / bad samples have shown the importance of good test samples for correct results.

Evaluation Part 1

From a customer, Seidenader received for initial testing a set of 200 samples in total, consisting of 100 samples which a leak test machine installed on the customer's premises had classified as good, and 100 samples which had been evaluated by the same machine as leaking. Once the test bench had been set up using the good products, the bad samples were inspected. But to the surprise of both Seidenader's developers and the customer, none of these samples were able to be detected as bad: all the samples were found to be satisfactory. A blue dye test (see figure 5), which was carried out on the customer's premises, then provided the explanation: not one of these samples showed discoloration, all the samples were airtight!

Evaluation Part 2

The customer himself then produced bad samples. By way of example, the test results for these samples in respect of tip defects are shown in figure 3. The red line represents the limit value for the pass/fail decision, which was determined as follows:

Using a large number of good product measured values (x), the average value μ and the standard deviation σ were determined, then the value μ+4σ was defined as the threshold. Assuming a normal distribution, there is therefore a false reject rate of less than 0.004%. In the tests, no false rejects at all were found and all bad samples were detected as bad with a very good level of discrimination. On the basis of this result the customer ordered a machine and then another one shortly afterwards. Further tests followed with specially prepared samples; the results confirmed the customer had made the right decision.

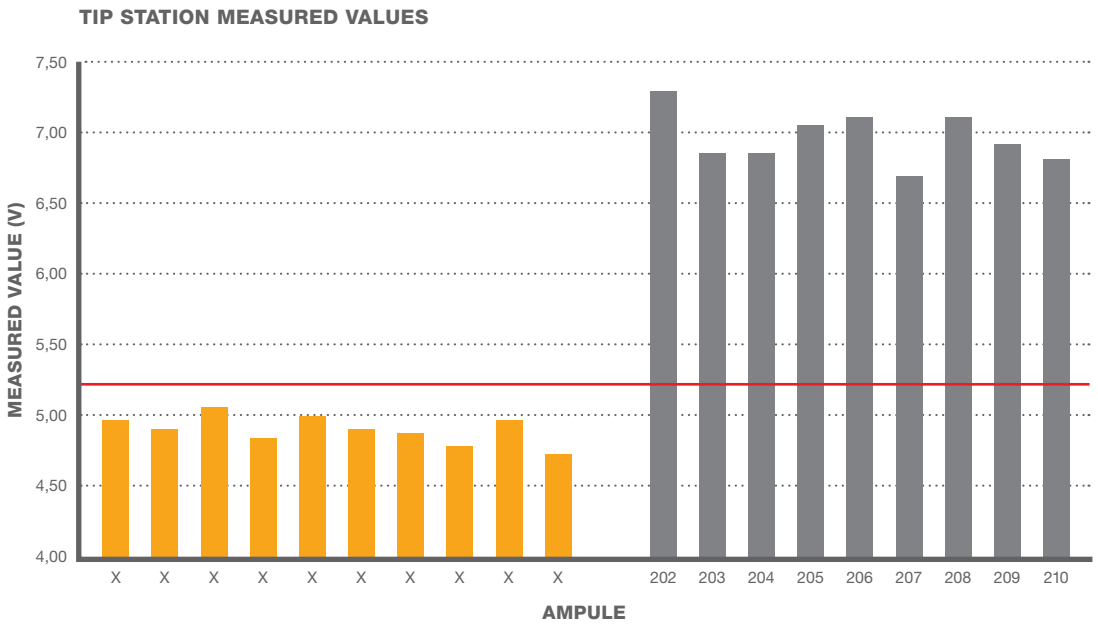

Fig. 3:
Tip inspection - Measured values for good products (left) and bad products (right)

HVLD

Fig. 10: *Dummies – metal core with powder coating*

THE DEVELOPMENT

Defective dummies

Since genuine defective samples do not exhibit long-term stability – the cracks may become larger or may close, the liquid runs out… – dummies had to be designed to provide evidence in principle of the system's functionality.

The design of these dummies was optimized in several stages. In the final version, each dummy has a metal core in the form of the respective container and is provided with a powder coating (figure 10). This coating gives the dummies a very resistant surface and the metallic cores are provided with the necessary electrically insulating coverings. In the case of good samples, the powder coating remains intact – for the defective samples a hole is through the insulating covering to the core and a metal pin inserted into it at the location where the defect is intended to be. In this way specific defects can be generated for the functional testing of each individual HVLD station.

Calibration

Further work has been done on calibration: for the current models, both the HV circuit and the measurement circuit of each HV station can be calibrated simply and if necessary re-adjusted using software parameters. Calibration is carried out every six or twelve months – entirely at the customer's discretion.

Is HV inspection suitable for all products?

One question which is often asked is: "Isn't the product affected by the impact of the high voltage?" Seidenader cannot answer this question. However, we offer to carry out degradation tests. For these tests, a sufficient number of identical samples (i.e. from the same batch) must be provided by the pharmacist. Some of these samples (Group A) remain untreated; a second group (Group B) is subjected to "normal" HV inspection. A third part (Group C) is inspected at a higher voltage and/or subjected to longer HV exposure. If necessary, intermediate stages can also be introduced here. After this procedure the samples are returned to the pharmacist, who then examines whether the products have been affected.

If all three (or more) groups emerge from the procedure without damage, HVLD is an appropriate procedure for this product. If Group B is not damaged, but Group C is, further tests must be carried out to determine whether there is an adequate "safety margin", i.e. whether the products can be inspected without risk of degrading them.

If B and C are damaged, but not A, this would mean that the products are being affected by the inspection. If all three groups are damaged, understandably no conclusions can be drawn about the effect of HV inspection.

Such tests have been carried out for various customers. In none of the cases to date – some including vaccines – damages caused by HV inspection were detected. Nonetheless, of course, it must not be generalized on the basis of this result.

Ongoing development

Despite all these positive aspects, work is incessantly being done to further develop the system. This will ensure that the system will continue to meet the requirements of customers and the market in the future.

More information ▸

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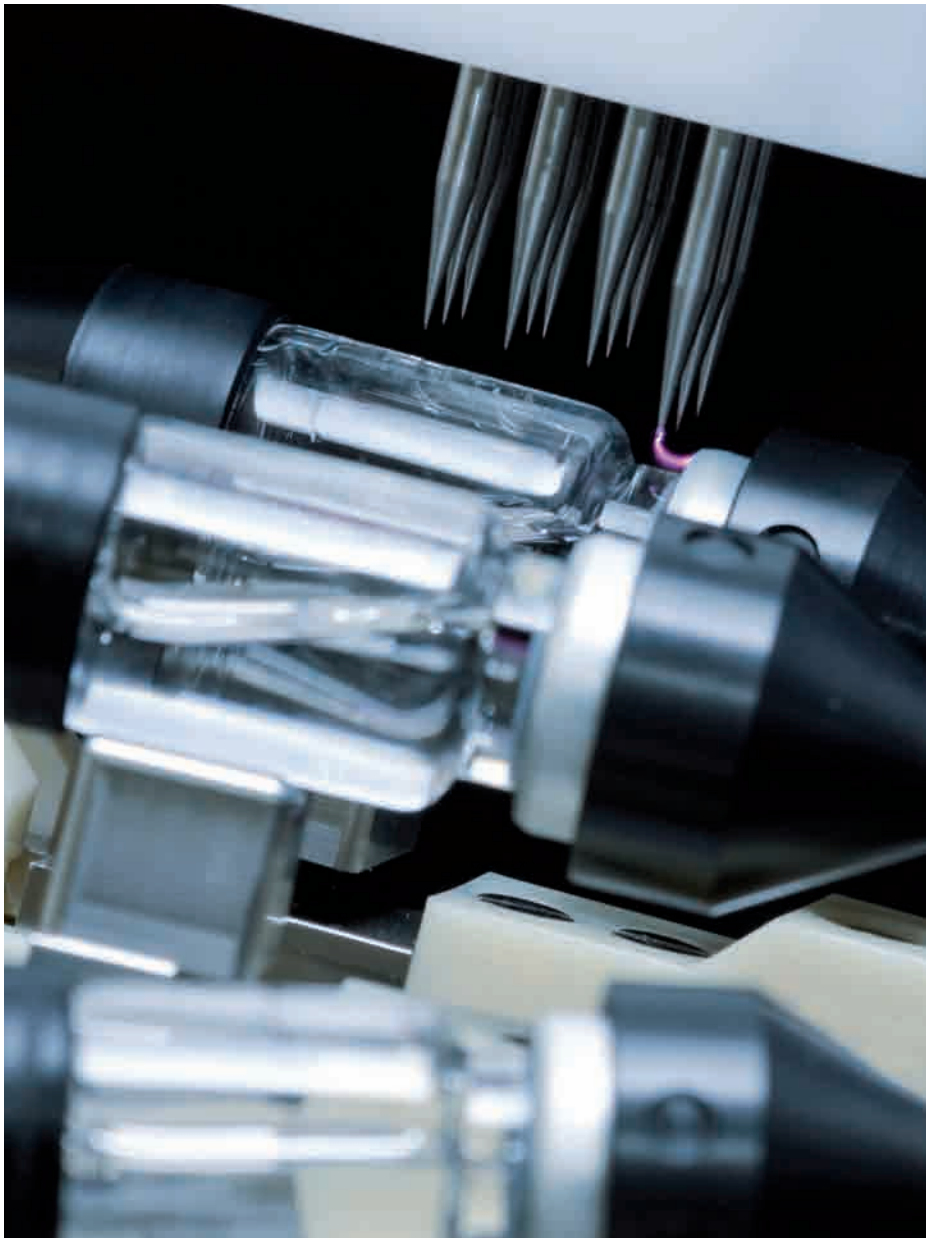
SEIDENADER
KÖRBER SOLUTIONS

CASE STUDY

HVLD – HIGH VOLTAGE LEAK DETECTION

With the introduction of high-voltage leak detection (HVLD), Seidenader Maschinenbau GmbH has extended its portfolio of high-speed inspection of pharmaceutical containers.



AT A GLANCE

CHALLENGE

A combination of camera inspection and high-voltage leak detection in one machine.

SOLUTION

High-voltage module for leak detection with precise product handling and reliable 360° inspection for integration into existing high-speed machines.

BENEFITS

- Low personnel costs
- Reduced maintenance costs
- Small footprint
- Lower investment costs

KEY WORDS

Container integrity, sterility of parenteral products, patient safety, 100% inline inspection, leak testing, high voltage, product quality.

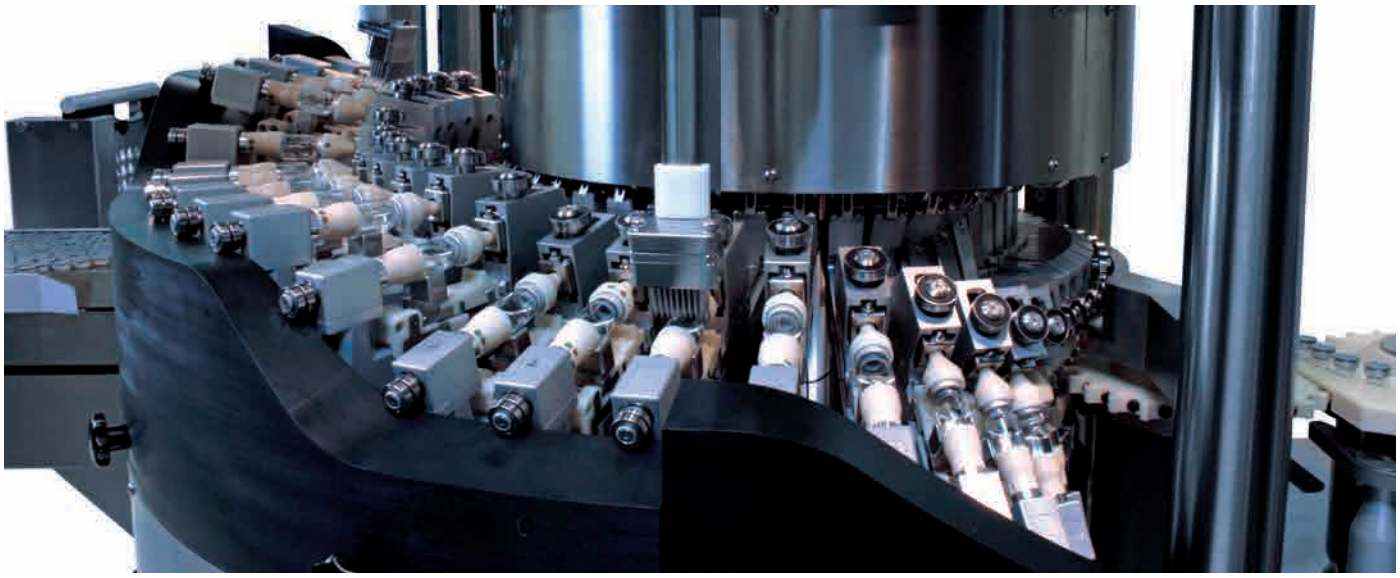


Fig. 1: *Product transport, sidewall inspection*

THE TECHNOLOGY

More and more attention is being paid to the integrity of pharmaceutical containers, because apart from the penetration of oxygen and its possible reactions with the product, the loss of sterility of parenteral products (e. g. injections, infusions) is the most serious threat to the health of patients.

High-voltage technology is used to detect the smallest cracks and pinholes in the sidewall, bottom and closure zone of pharmaceutical containers, provided that the product has a minimum electrical conductivity. The object which is to be inspected is brought between electrodes to which an alternating high voltage is applied. It becomes part of an HV circuit (see figure 2) and, together with the electrodes, represents an electrical resistance in this circuit. Damage to the object, such as cracks or leaks, leads to a reduction in resistance and hence to an increase in the flow of electrical current. This change is detected and analyzed using instrumentation. A comparison of the measured value with previously determined limit values for good objects then provides an indication of whether the object is satisfactory in terms of the HV inspection.

Seidenader can look back on several years of successful application of this procedure.

THE INTEGRATION

The decisive factors in this context were on the one hand the integration of HV technology into camera-based vision inspection machines and on the other hand innovative product transport, which from the start significantly distinguishes Seidenader HVLD machines from its competitors' machines. Thus for the bottom inspection, the products are held, perfectly defined, in a vacuum star wheel, so the distance both from the needle electrodes and the earth electrode is kept constant within very tight tolerances. For the sidewall inspection (see figure 1) the product is centered and secured top and bottom and is able to be rotated accurately; on the one hand this ensures a precise distance of the product from the electrodes and on the other hand accurate 360° rotation of the product in front of the HV electrodes. In addition, precise product handling also makes it possible to map the contour of the test objects with the electrodes, which is also reflected in the high defect detection rate. For the inspection of low fills, a specially developed pivot carousel enables products to be tilted beyond the horizontal for complete wetting of the sidewall and the area around the seal.

These innovative design details aroused considerable interest in this technology among several customers, even during the development of the first prototype.

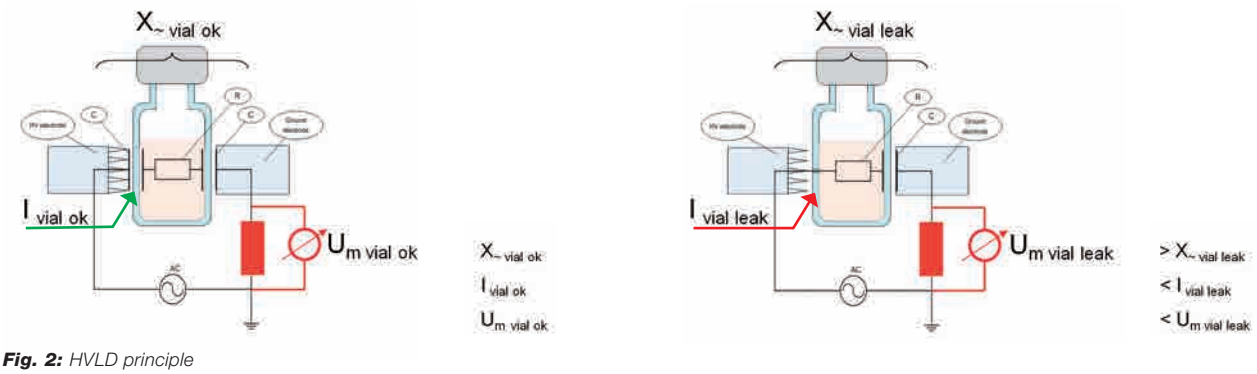


Fig. 2: *HVLD principle*

TEST METHOD	USP/PhEur	ISO	Seidenader
dye solution methylene blue concentration	0.1 %	0.1 %	1 %
vakuum	-270 mbar	-250 mbar	-850 mbar
time@vacuum	10 min.	30 min.	5 x 5 min. = 25 min.
time@atmospheric pressure	30 min.	30 min.	60 min.
dye verification method	visual	visual	visual

Fig. 4: *Seidenader made the specifications of the blue dye test even more stringent than USP (United States Pharmacopeia) and PHEur (Pharmacopoea Europaea)*

THE COMPARISON

Accepted integrity test: vacuum decay method

This experience has shown that it is important to provide a broadly accepted basis of comparison in order to demonstrate the efficiency of the system. The helium leakage test is a very good and quantitatively reliable method. However, the procedure is very expensive. The vacuum decay or pressure decay method is somewhat easier to apply, but it does have certain limitations. The above-mentioned blue dye test is the simplest and most convenient – although it does have other disadvantages. This procedure was adopted by the customer as a reference. It is a common procedure accepted by pharmacists – but it is not suitable for production applications.

In this test the samples to be inspected are immersed in an intensively blue solution (methylene blue) (see figure 5). This blue bath is then subjected to a partial vacuum. This causes leaking samples to be evacuated. Consequently, when the system is then ventilated, methylene blue is sucked into the defective sample which is subject to the partial vacuum. During the subsequent inspection, the bad samples are detected because of their blue coloration. Naturally, it is samples with colorless, clear and liquid contents that are mainly suitable for this test.

Blue dye test versus HVLD inspection

For the “Seidenader blue dye test” the specifications of the USP (United States Pharmacopeia) and PhEur (Pharmacopoea Europaea) are made even more stringent (see Figure 4). Cracked vial samples were prepared and initially inspected using HVLD. These samples were then subjected to the blue dye test. The results are shown in figures 7 to 9: Various defect positions are represented on the abscissa; the ordinate shows the respective detection rate – in orange for HVLD and in blue for the blue dye test. The dark-colored part in each case concerns those samples which were detected using both methods; the lighter part above shows those samples which were detected by only one method. Of the total of 315 samples produced, 115 were not detected as bad by either of the two methods (value in figure 6 bottom right).

It has to be assumed that these presumed cracked samples were actually tight. In this regard, it is also not surprising that some of the detection rates in figures 7 to 9 are well below the 100% mark. It is, however, clearly evident that HV inspection detects significantly more defective samples than the blue dye test.

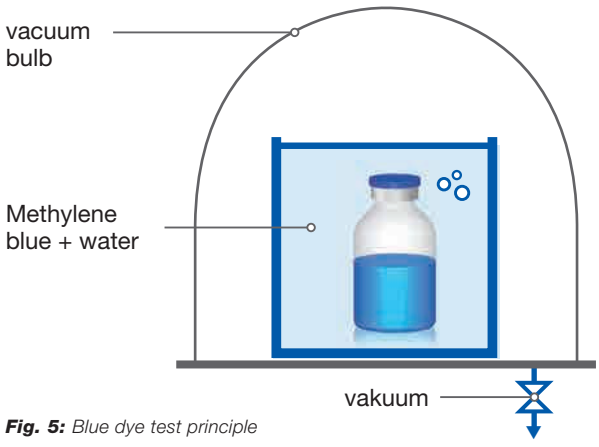
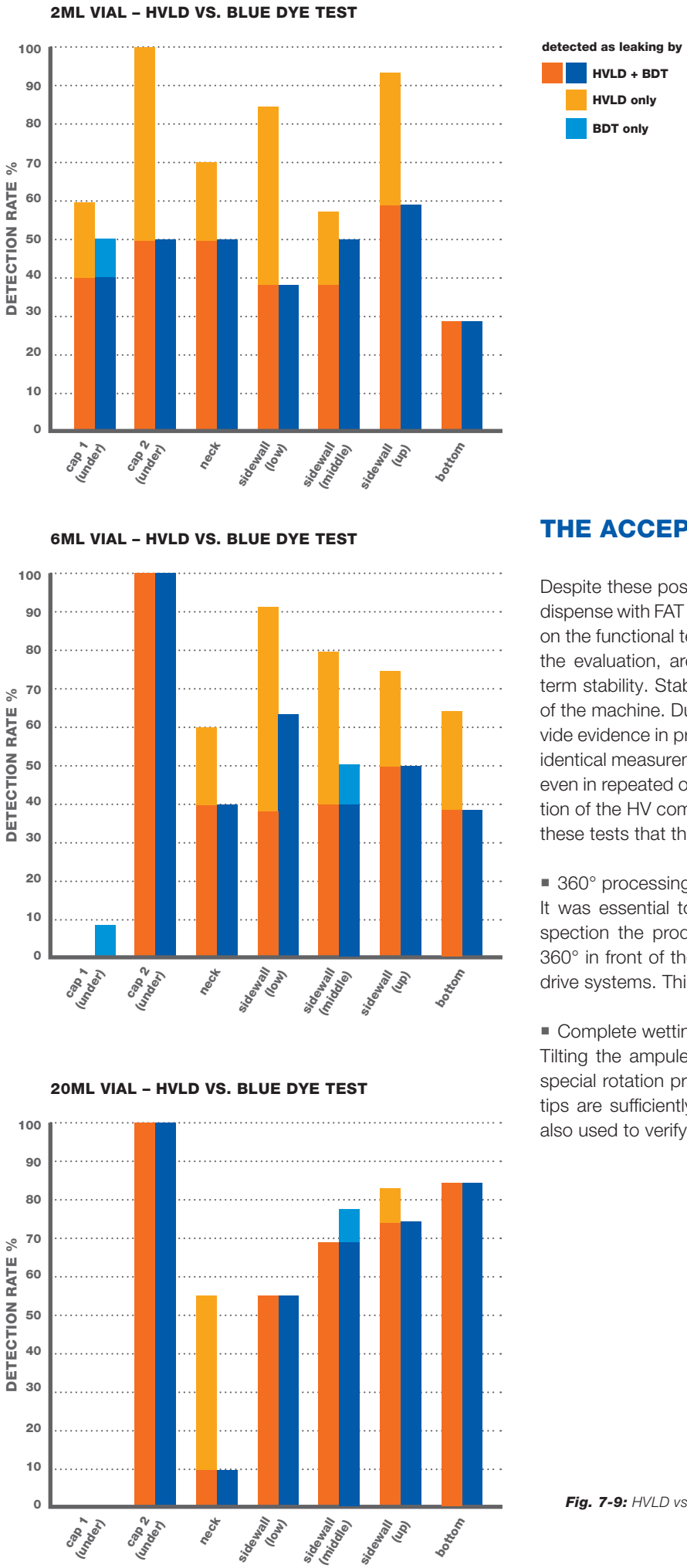


Fig. 5: *Blue dye test principle*

Cracks are ...	... identified by HVLD: **98 %**	... not identified by HVLD
... identified by BDT: **71 %**	69 % (fracture which penetrates the glass wall)	2 % Cracks that are opened when applying vaccum
... not identified by BDT	29 % cracks that are closed when applying vacuum	115 samples! Probalby no cracks – defects do not penetrate the glass wall (checks or scratches)

Fig. 6: *HVLD vs. blue dye test*



THE ACCEPTANCE

Despite these positive results, it was naturally not possible to dispense with FAT and SAT tests. In this context, the focus was on the functional test. Genuine defective samples, as used for the evaluation, are unsuitable, as they do not exhibit long-term stability. Stable conditions are essential for the approval of the machine. Dummies are therefore generally used to provide evidence in principle of the system's functionality; virtually identical measurement results are always achieved with these, even in repeated operation. However, in addition to the operation of the HV components, it also had to be demonstrated in these tests that the mechanical conditions are met:

- 360° processing

It was essential to demonstrate that during the sidewall inspection the products are actually rotated through at least 360° in front of the HV electrodes by the individual rotational drive systems. This was verified using video recordings.

- Complete wetting

Tilting the ampules at more than 90°, in conjunction with a special rotation profile, is intended to ensure that the ampule tips are sufficiently filled and wetted. Video recordings were also used to verify this function.

Fig. 7-9: *HVLD vs. blue dye test, demonstrated on vials of different sizes*