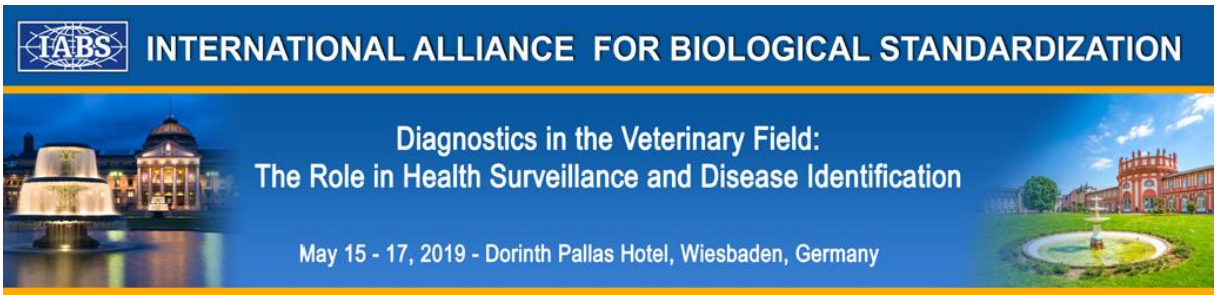

CONCLUSIONS AND RECOMMENDATIONS

Conclusions:

- Diagnostic tests are performed for:
    - Point of care purposes to evaluate the health status or immunological status of certain individual animals or groups of animals
    - Endemic disease diagnosis to support health management decisions and medical interventions
    - Disease surveillance and freedom from notifiable diseases by official control laboratories. Test performance expectations are very high for diagnostics for outbreak investigations of transboundary (notifiable) diseases or eradication programmes
    - Confirmation of disease-free status, tied to ongoing disease surveillance and confirmation of trade status
    - High quality diagnostics are important for
        - the detection of pathogens,
        - epidemiological investigations,
        - detecting changes in disease situations,
        - use of results by Animal Health Authorities.

- Testing objectives include:
    - Routine surveillance of health status including freedom from disease
    - Diagnosis of emerging and other diseases
    - Disease eradication initiatives [including vaccine/DIVA (Differentiation of infected animals from vaccinated animals) strategies].
    - Testing food, feed, and the environment for pathogens and for antimicrobial resistance genes
    - Testing of vaccines for performance, potency, and quality.

- The current quality spectrum of tests is:
    - Evolving, especially with the application of new technology.

    - Most methodologies can be considered as good (but not perfect) especially in cases where there is a lack of standardised methodologies.
    - Validated to certain stages, differing from test method to test method and manufacturer to manufacturer (exceptions include kits under the control of a National Regulatory Authority).
    - Test to test comparison across similar products is challenging e.g. due to different sensitivity/specificity. There is often a gap in test capabilities by users.

- Test methods:

    - In addition to “classical” tests which have and will continue to have their place in diagnosis of all kind of health surveillance, new methods come in. The value of classical serologic tests, some of which have been in use for more than 150 years is recognised, even if the number and capabilities of new molecular tests is broad and growing. As always, greater confidence regarding test interpretation comes with greater experience in using the methodology under diverse real-life situations

    - An increasing number of tests systems are becoming available on the market including those intended for frontline use by persons with no or little experience in lab tests.

    - Newer molecular diagnostic tests can be extremely valuable tools in animal health systems, especially in the ability to test for multiple pathogens (multiplexing) and improving testing result timelines. Rapid tests can serve as early warning tools and free time to enhance biosecurity and vaccinate to contain outbreak. Complex infections are common – what is the clinically relevant agent and what is adventitious?

    - New diagnostic methodologies also have application to vaccine purity, safety and potency performance. The diagnostic methods also inform on the need for intervention (variety of measures) to public health.

    - The routine sequencing of a relevant/small part of one gene may however cause confusion: what does a certain mutation mean? Decisions have to be made case by case, often supplemented by field observations and disease agent characterisation using additional methodologies.

    - Sequencing is an excellent tool for molecular epidemiology and provides easy availability of big data. Real understanding of data provides a good opportunity to identify epidemiological threats.

    - The use of representative control samples is regarded as essential. One positive and one negative sample per test run may be insufficient to reflect

the variety of samples in the field. There is value in testing control samples with varying levels of response to confirm test performance and facilitate interpretation.

- Use of diagnostics:
    - There is a permanent challenge with having the right sample/specimen sent in the right way to laboratories – this shows the need for better communication to vets and farmers, and better education of vet students in diagnostics.
    - For frontline use vets and farmers need support to analyse these data quickly and easily to allow immediate decisions on further action.
    - Disease prevalence, clinical relevance, and “fitness for purpose” need to be considered when choosing a diagnostic test, especially for emerging and notifiable diseases.
    - Sequencing (genotypes) does not necessarily indicate pathotypes and serotypes.
    - Cost/affordability of individual tests is a significant factor in the use of the diagnostic methodologies
- Diagnostics and vaccination
    - Development of DIVA vaccines and diagnostics simultaneously is ideal, but not always realistic. Experience tells us that a non-differentiable vaccines can be developed faster than a differentiable vaccines (with an accompanying diagnostic test kit or technology).
    - Cooperation between vaccine producers and diagnostics producers is needed, since DIVA strategies are requested by the public and politicians more and more, and because stamping-out strategies are not publicly acceptable anymore. The earlier the overall disease control/management objective is understood, the better vaccination/test strategy can be developed, so products can be tailored to the need.
- Trade and animal movement:
    - Understanding the test expectations and limitations is critical when interpreting results. The issue of the impact of “false positives or false negatives” on trade or animal movement is similar with any testing methodology (old/new, traditional/molecular). Understanding the test expectations and limitations is critical when interpreting results.

- Confirming results for the diagnosis of controlled (notifiable) diseases via that National Authorities Testing Laboratory remains as a critical step in the diagnostic process and must serve as the basis for decisions on disease management, e.g. culling/reimbursement.

- Official approval / licensing

  - Diagnostic tests must be “safe” and sound, so we can rely on the findings. A consistent approval process by authorities will serve this goal. Currently, the lack of EU approval is compensated by the cooperation and validation performed by many reference laboratories (EU and national). In USA licensing is established. Technical expectations for authorisation data vary by country, complicating test development and approval.

  - Well-coordinated laboratory networks are critical to national, regional and international animal health. OIE/FAO continue to provide proficiency testing for Foot-and-Mouth disease (FMD) and other diseases, which is expensive, but important. E-learning courses may also be useful. The international ISO requirement for proficiency testing should come into force.

  - Proficiency testing of reagents are not enforced/applied. There may be a huge variability in potency of reagents even in marketed products that claimed to conform to OIE requirements, which could have a disastrous effect on a disease control program and lead to a general mistrust of test results.

  - The variability of the regulatory scrutiny of veterinary diagnostic tests across the world is very large, ranging from strict authority licensing and control to no official regulation at all. This may impact on international trade due to variable requirements.

Recommendations:

- Official approval / licensing
    - There is an urgent need for international harmonisation of quality requirements and licensing procedures. Setting of common standards on the quality of manufacture and validation of test systems is needed.
    - Propose that the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Products (VICH) consider asking to extend their mandate by laying down technical requirements for diagnostics. This should take into consideration the already existing OIE relevant Chapters of the Manuals (1.1.6 of the Terrestrial and 1.1.2 of the Aquatic Manual).
    - Establish licensing procedures to ensure a defined level of quality, validation, storage and transport conditions and follow up procedures to evaluate the performance of test systems in the field. The authorities should take steps to ensure that approval/license is withdrawn when license conditions, stipulations and label claims are not met, and that that such products are taken off the market.
    - Compliance with internationally agreed upon OIE diagnostic methods (Manual of Diagnostic Tests and Vaccines for Terrestrial Animals and Manual of Diagnostic Tests for Aquatic Animals) is essential. Proof of compliance needs to be provided by the relevant labs.

      The OIE network should be used to pool resources for serum and sample banks, outbreak response, and R&D coordination. Feedback should be sent back to OIE-reference labs. The existing OIE procedure, which was adopted by the OIE Member Countries, could be used as a tool for registration of diagnostics.
    - For the EU, a common licensing procedure should be established (Decentralised or Centralised procedure). This also applies to other regions without a licensing procedure. BUT: quick reactions to immediate threats must be ensured.
    - The OIE Procedure contains a paragraph which allows a provisional registration, which might be further elaborated in the future.
    - New developments require quick and facilitated licensing procedures to make better methods quickly available to all users especially in emergency situations, e.g. next-generation sequencing approaches should be integrated into diagnostic workflows including validation of test performance, where applicable.

- Establish official written and physical standards for calibration of test systems. This will allow the mutual recognition of physical test results within the network of official control labs and ensure the use of identical test kits within the regions where tested animals are moved.

- Retesting of commercially available test systems by official laboratories to confirm consistency of test results. Clear information should be available for the test user/buyer on the test's performance, limitations, and interpretation of results. Results to be published comparable to the public assessment reports (PuARs) issued by EMA.

- Quality of diagnostics

  - Diagnostic test kit development is challenging but should include:
    - validation against the current "gold standard" test provided it is applicable or available,
    - minimizing false positive and false negative results,
    - ensuring repeatability,
    - sample preparation,
    - skills and capability of the test operator.

  - Test Validation (sensitivity, specificity, repeatability, target population) is critical as is manufacturing quality control and oversight by Regulatory Authorities. Distinguish peace time and emergency licensing to ensure the quick availability of urgently needed test systems, and tailor the regulatory scrutiny to the risk.

  - Define the scope of a particular test systems in terms of sensitivity, specificity, (percentage of false positive and / or negative results). The scope should differ between endemic, exotic, and notifiable diseases and consider interfering infections.

  - The growing number of new pen-side tests for pathogen detection and serology should be validated through the established networks of reference laboratories and their partners.

  - (New) diagnostic methodologies must have sufficient discriminatory power and be robust enough to be used within a testing system.

- Use of diagnostics

  - There is a need to understand what the method actually delivers to ensure proper usage of the data.

- Establish a system of quick data transfer from the field to official control labs for verification, in particular when notifiable diseases are concerned.

- Multi-parameter testing, such as a battery of test methodologies; or point-of-care versus in-laboratory tests, has the potential to improve diagnostic certainty. For example, point-of-care data may help exclude conventional pathogens, expediting decisions to initiate controlled agent testing by national laboratories.

- In the Diagnostic Industry “Big Data” are upcoming, where standardized processes to handle and secure these “Big Data” available from different technologies are needed.

- When considering the risks associated with transboundary diseases, testing samples other than animal samples such as fomites and the environment need to be considered. Newer information indicates that feed may be a higher risk for spreading of pathogens than previously anticipated, especially for products (e.g., feed) moving long distances internationally.