Regulatory framework and requirements for managing risks associated with veterinary biological products in Africa: present systems and future needs

D. SYLLA *, M.M. RWEYEMAMU ** and V.J. PALYA **

Summary: Veterinary vaccines are considered to be medicinal products. As such, they are subject to assessment for managing risks associated with their marketing and use. The current risk assessment procedures used in Africa are based on the quality testing methods standardised by the Pan-African Veterinary Vaccine Centre (PANVAC).

The authors examine the risk assessment procedures related to the importation of products and to the release of live products into the environment. The lack of infrastructures, specialised personnel and financial resources prevents each individual country from establishing its own system for managing the risks associated with the importation of veterinary vaccines. Regional co-operation between African countries is therefore recommended, and must be based on the existing PANVAC network for the quality testing of priority vaccines. This is justified by the results obtained by PANVAC in the standardisation of production technologies for vaccines against rinderpest and contagious bovine pleuropneumonia, and in other areas.

The authors recommend that PANVAC be used to aid regional co-operation in Africa in the management of risks associated with the marketing and use of veterinary vaccines.


INTRODUCTION

Products used for the treatment or prevention of human or animal diseases are medicines. Biological products used either as vaccines or as therapeutic agents are generally regarded as immunological veterinary medicinal products (IVMPs). They are expected to be effective in their intended use, and use must be governed by the principle of 'primum non nocere', i.e. the prime requirement of IVMPs is that they shall do no harm to the recipient, contact animals or human handlers, and should result in no harmful

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residues either in food products derived from recipient animals or in the environment. The preparation, handling, marketing and use of vaccines should be regulated to protect the treated animals, the persons handling the medicine, the consumers of treated food animals and the environment. Regulatory mechanisms are or should be in place to license such products and ensure that IVMPs conform to standards of safety for animals and the public, and of quality and efficacy for the intended use. Rutter (12) has defined these attributes as described below.

Safety

Safety is interpreted in a broad sense, to include the following:
- the animal being treated
- in-contact animals
- the user (e.g. the veterinarian, farmer or pet owner administering the medicine)
- the consumer of livestock products from treated animals
- the environment.

Quality

Quality means that medicines (vaccines) must be manufactured with appropriate quality control procedures, in premises which are inspected and licensed; the ingredients must be of appropriate purity, in the correct proportions and correctly processed; the containers must be robust, with secure closures; the labelling must be accurate and informative.

Efficacy

Efficacy means that medicines (e.g. vaccines) must correspond to claims made by the manufacturer, i.e. they must be effective against the designated disease(s), in the intended species of animals, and using the recommended dose rate, frequency and duration of treatment, and route of administration.

Soulebot et al. (17) have argued that, in developing countries, quality assurance and 'good manufacturing practice' (GMP) are probably even more important for veterinary vaccines than for pharmaceutical (i.e. chemical) products. This thesis is based on the following considerations:
- the active ingredient for vaccines is almost always produced by the vaccine manufacturer
- vaccine production involves a cultivation step (i.e. amplification) and the use of substances of animal origin
- vaccine manufacture involves handling of live organisms, which are sometimes highly pathogenic for animals or humans
- there is no terminal sterilisation.

Ironically, closer attention is paid to the risks of contaminant hazards in developing countries than in industrialised countries. A contributing factor is that infectious and blood-borne diseases are of greater significance in developing countries in tropical and sub-tropical regions than elsewhere (7, 15, 6). Another paper in this issue of the Scientific and Technical Review of the Office International des Epizooties (OIE) describes risk factors associated with the use of biological products in developing
countries (18). The present paper therefore concentrates on the need for appropriate regulatory mechanisms, drawing largely from the experience of the Pan-African Veterinary Vaccine Centre (PANVAC).

**EVOLUTION OF THE PAN-AFRICAN VETERINARY VACCINE CENTRE**

PANVAC was founded due to the need for effective regional control of rinderpest. In Africa, three major cycles of rinderpest campaigning have been coordinated on a regional basis. The first of these, in the 1930s and 1940s, involved the countries of Southern Africa which now constitute the economic bloc known as the Southern African Development Community (SADC: comprises Angola, Botswana, Lesotho, Malawi, Mozambique, Namibia, South Africa, Swaziland, Tanzania, Zambia and Zimbabwe). Veterinary officers from these countries formed brigade teams drawn from the countries in the region, to perform mass ‘vaccination’ (essentially using serum virus) until rinderpest was ‘banished’ to north of the Central Railway line in Tanzania (3). The second campaign (known as Joint Programme 15: JP15) was conducted between 1962 and 1976, with the aim of controlling rinderpest throughout the continent (1). JP15 differed from previous regional or national attempts at rinderpest eradication, as it was based on mass application of a newly-developed cell-culture vaccine (11), which had been shown to be safe for all breeds of cattle. Previously, the most widely used vaccine was that derived from goat spleen tissue which had the drawback of post-vaccinal reactions, even causing clinical rinderpest in cattle of low innate resistance (10) or exacerbating concurrent infection with haemoparasites (8, 16). Therefore, JP15 aimed to provide maximum benefit (rinderpest control) at minimum risk, through the use of a safe vaccine.

At the end of the JP15 campaign, pockets of rinderpest were known to persist in Africa. The expectation was that these areas would be eliminated by national follow-up actions. Hindsight shows that the extent of residual endemic rinderpest was probably underestimated, and that follow-up measures by national governments were grossly inadequate. Consequently, major resurgences of rinderpest occurred in the early 1980s. During this period, the Food and Agriculture Organisation of the United Nations (FAO) was flooded with requests for emergency assistance to combat rinderpest, and it was therefore apparent that rinderpest had attained transnational and pandemic proportions. In addition to short-term emergency interventions (national and regional Technical Co-operation Programme projects between 1979 and 1981), the FAO and the OIE organised a series of workshops and expert consultations, most notably the 1984 Expert Consultation on Rinderpest Diagnosis and Vaccine Production, and the 1986 Expert Consultation on the Feasibility for Global Rinderpest Eradication. One of the key recommendations of these consultations was that it was essential to verify the quality of rinderpest vaccine to be employed in this new campaign: the Pan-African Rinderpest Campaign (PARC). Thus, in 1985, samples of vaccine were collected from 13 national vaccine laboratories, which were producers of rinderpest vaccine; these samples were subjected to external, independent quality control by FAO reference laboratories in Europe and Africa. Most samples failed to attain the required level of potency, and many also failed in sterility. The risk associated with such vaccines was that they would fail to meet expectations of efficacy (i.e. fail to protect cattle against rinderpest) and that they were hazardous as injectable medicinal products, because of the risk of contamination.
This prompted the Organisation of African Unity to request the FAO to assist in setting up a system for independent quality control of rinderpest vaccine. Initially, this was achieved through short-term assistance under the FAO Technical Co-operation Programme (in 1986) by establishing a unit at the National Veterinary Institute in Debre Zeit, near Addis Ababa (Ethiopia) and another at the Laboratoire national d'élevage et de recherches vétérinaires in Dakar (Senegal). In 1988, this effort was further aided through a project funded by the United Nations Development Programme (UNDP), namely UNDP/FAO/RAF/88/050, which supported both units until the end of 1992, by which time the two units formally constituted PANVAC. During 1993, it was decided to merge the two units and perform the functions of PANVAC at one site in Debre Zeit (Ethiopia). This was dictated by the lack of immediate funds, but more importantly by the need for a sustainable structure after the project phase. Beginning in 1995, PANVAC will commence a system of cost recovery for quality control services, with the financial support of the European Union and technical assistance from the FAO. This will be achieved by charging vaccine producers a commercial rate for quality control.

MANDATE OF THE PAN-AFRICAN VETERINARY VACCINE CENTRE

The mandate of PANVAC is four-fold, as follows:

a) to provide international quality control of priority vaccines

b) to promote the concepts of biological standardisation and control in Africa

c) to transfer appropriate vaccine production technologies to Africa (including adaptation or development to suit African conditions)

d) to provide training in vaccine technology, and methods for production and quality control.

VACCINE QUALITY CONTROL

Testing was initially instituted to assess the quality of emergency vaccine stocks held by PARC in five designated vaccine banks. At first, the two units performed tests for vacuum, potency (titration) and sterility of the vaccines. As the PANVAC programme has been consolidated, the range of quality control testing has expanded. The programme has gradually reached a stage where PARC is requesting all Veterinary Services under the programme to purchase only PANVAC quality-certified rinderpest vaccine. This position has been endorsed by the Chief Veterinary Officers of the 34 PARC member countries.

Production laboratories

When PANVAC testing began, thirteen countries in Africa were producing rinderpest vaccine, while now only ten are in active production. Table I lists the rinderpest vaccine production laboratories in Africa and the latest available annual production data. Four countries – namely Botswana, Cameroon, Ethiopia and Kenya – account for approximately 75% of the total annual production of rinderpest vaccine in Africa.
One peculiarity of Africa is the almost total absence of private, commercial enterprise in vaccine production. Only one international vaccine manufacturing company has a manufacturing facility in Africa, which is jointly owned by the host government. In other countries, fully government-owned companies have been established, which are responsible for the production and marketing of all veterinary vaccines. Elsewhere in Africa, vaccines are produced by the state veterinary departments themselves, although in a number of countries there are moves to set up vaccine production sections as self-accounting units.

Vaccines

All producers employ the cell-culture technique and the Kabete O (RBOK) strain of Plowright. Originally, only the calf kidney cell culture-adapted virus was employed. At PANVAC, an FAO reference virus bank was set up with the help and co-operation of the Institute for Animal Health in Pirbright (United Kingdom), and the virus has been designated as follows:

- FAO International Rinderpest Reference Virus
  Kabete ‘O’, BK95.

In 1991, through the collaboration of the Plum Island Animal Disease Centre (Long Island, New York), Tufts University (North Grafton, Massachusetts) and PANVAC, a Vero cell adapted virus was introduced into some national vaccine production laboratories. This has been designated as follows:

- Rinderpest Vaccine Production Seed
  Plowright Strain, 92BK 4VERO
  United States Department of Agriculture, Animal and Plant Health Inspection Service, Foreign Animal Diseases Diagnostic Laboratory (FADDL).

Recently, another Vero cell adapted virus known as the ‘thermostable rinderpest virus clone’ was tested by the Centre de coopération internationale en recherche agronomique pour le développement/Département d’élevage et de médecine vétérinaire (CIRAD/EMVT) in Paris and this has been distributed to a few production laboratories. This virus has been designated as follows:

- Peste bovine, Thermo Vac
  Banque de semence
  98RV – 12 Vero

Primary/secondary calf kidney cells were the traditional substrate for vaccine production. Since 1990/1991, however, producers in all but two countries (Chad and Sudan) have switched to the use of Vero cells.

Sample collection

When testing first began, vaccine samples were hand-carried from the production laboratory to the PANVAC laboratories. Since then, through the host country agreements, vaccine producers are able to submit vaccine samples to PANVAC by normal parcel postage/courier service, and PANVAC has the privilege of being able to clear such parcels through customs promptly. Experience has shown that vaccine samples should be clearly marked, and should be refrigerated at the airports in case of possible delay. Consequently, there have been no cases of vaccine spoilage in transit.
In 1990, a PANVAC vaccine submission form was distributed to all manufacturers, and each submitted batch should now be accompanied by a duly completed form.

**PANVAC quality control testing procedure**

PANVAC has standardised the quality control testing of rinderpest vaccine to levels comparable with those of the British and European Pharmacopoeia standards, the OIE norms for rinderpest vaccine, and the procedure of the Veterinary Medicines Directorate in Weybridge (United Kingdom) for the control of bovine live viral vaccines.

A manual detailing the ‘standard operating procedures’ (SOP) for rinderpest vaccine quality control testing has been prepared and distributed to vaccine producers in Africa. This manual has now been published by the FAO (14).

The tests described in this manual include the following:
- test for sterility (bacteria, fungi)
- test for brucella (for seed materials)
- test for absence of mycoplasmas
- test for potency:
  - estimation of virus content
  - efficacy test in cattle
- test for thermo-stability
- test for rinderpest identity and adventitious agents:
  - staining of cell cultures by haematoxylin-eosin
  - test for haemadsorbing agents
  - test for bovine virus diarrhoea (BVD) virus by the immunoperoxidase method
- safety tests:
  - in laboratory animals (innocuity test)
  - in cattle.

**Evolution of vaccine potency**

Between 1988 and 1993, PANVAC tested a total of 694 batches of rinderpest vaccine, comprising 517 batches of vaccine against rinderpest alone and 177 batches of combined vaccine against rinderpest and contagious bovine pleuropneumonia (CBPP). Tables I and II present the potency data for each rinderpest vaccine producer in Africa, while Tables III and IV show the statistics for the batches which passed PANVAC quality control testing, and were therefore released for use in PARC. In contrast with results obtained during the initial stages of the programme, these results show that most vaccine producers in Africa readily attain the OIE minimum requirement of a titre of 2.5 log_{10} TCID_{50} (50% tissue culture infective dose) per cattle dose.

**Analysis of the causes of vaccine failure**

Table V depicts the causes of rinderpest and combined rinderpest/CBPP vaccine failures encountered in Africa.

Lack of potency has evidently been the most frequent cause of failure. Increasing use of Vero cells in rinderpest vaccine production, however, has resulted in the improvement of vaccine potency and a subsequent reduction in the number of failed batches. Nevertheless, other causes of failure must also be considered. Sterility seems to cause less
<table>
<thead>
<tr>
<th>Parameter</th>
<th>MB-8</th>
<th>A-8</th>
<th>H-4</th>
<th>M-8</th>
<th>DAM-5</th>
<th>T-4</th>
<th>K-5</th>
<th>B-7</th>
<th>D-7</th>
<th>N-5</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of batches tested</td>
<td>96</td>
<td>18</td>
<td>27</td>
<td>41</td>
<td>164</td>
<td>94</td>
<td>14</td>
<td>9</td>
<td>7</td>
<td>38</td>
</tr>
<tr>
<td>Mean log_{10} titre per dose</td>
<td>3.553</td>
<td>3.381</td>
<td>2.388</td>
<td>3.053</td>
<td>2.749</td>
<td>2.859</td>
<td>3.491</td>
<td>2.425</td>
<td>3.188</td>
<td>2.440</td>
</tr>
<tr>
<td>Standard error of mean</td>
<td>0.041</td>
<td>0.102</td>
<td>0.184</td>
<td>0.090</td>
<td>0.065</td>
<td>0.063</td>
<td>0.139</td>
<td>0.174</td>
<td>0.345</td>
<td>0.075</td>
</tr>
<tr>
<td>Median</td>
<td>3.565</td>
<td>3.455</td>
<td>2.650</td>
<td>3.100</td>
<td>2.590</td>
<td>2.900</td>
<td>3.650</td>
<td>2.600</td>
<td>3.510</td>
<td>2.612</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>0.401</td>
<td>0.434</td>
<td>0.956</td>
<td>0.578</td>
<td>0.829</td>
<td>0.617</td>
<td>0.520</td>
<td>0.523</td>
<td>0.913</td>
<td>0.465</td>
</tr>
<tr>
<td>Minimum</td>
<td>2.630</td>
<td>2.650</td>
<td>0.600</td>
<td>1.830</td>
<td>0.360</td>
<td>0.500</td>
<td>2.600</td>
<td>1.830</td>
<td>1.500</td>
<td>1.490</td>
</tr>
<tr>
<td>Range</td>
<td>2.620</td>
<td>1.300</td>
<td>3.100</td>
<td>2.200</td>
<td>4.190</td>
<td>4.000</td>
<td>1.500</td>
<td>1.240</td>
<td>2.750</td>
<td>2.110</td>
</tr>
<tr>
<td>Skewness</td>
<td>0.655</td>
<td>-0.400</td>
<td>-0.714</td>
<td>-0.369</td>
<td>-0.007</td>
<td>-0.422</td>
<td>-0.359</td>
<td>-0.100</td>
<td>-1.041</td>
<td>-0.153</td>
</tr>
<tr>
<td>Kurtosis</td>
<td>2.746</td>
<td>-1.168</td>
<td>-0.653</td>
<td>-0.498</td>
<td>-0.491</td>
<td>2.403</td>
<td>-1.360</td>
<td>-2.293</td>
<td>1.117</td>
<td>-0.234</td>
</tr>
</tbody>
</table>

**Table I**

Statistical analysis of the potency results of rinderpest vaccine for each producer in Africa
Table II

<table>
<thead>
<tr>
<th>Parameter</th>
<th>A8-8</th>
<th>H-4</th>
<th>M-8</th>
<th>D-7</th>
<th>K-5</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of batches tested</td>
<td>34</td>
<td>43</td>
<td>33</td>
<td>60</td>
<td>7</td>
</tr>
<tr>
<td>Mean log_{10} titre per dose</td>
<td>3.753</td>
<td>2.605</td>
<td>3.409</td>
<td>3.059</td>
<td>2.086</td>
</tr>
<tr>
<td>Standard error of mean</td>
<td>0.067</td>
<td>0.072</td>
<td>0.075</td>
<td>0.076</td>
<td>0.547</td>
</tr>
<tr>
<td>Median</td>
<td>3.865</td>
<td>2.700</td>
<td>3.300</td>
<td>3.160</td>
<td>2.700</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>0.393</td>
<td>0.474</td>
<td>0.435</td>
<td>0.589</td>
<td>1.447</td>
</tr>
<tr>
<td>Maximum</td>
<td>4.450</td>
<td>3.450</td>
<td>4.060</td>
<td>4.150</td>
<td>3.400</td>
</tr>
<tr>
<td>Minimum</td>
<td>2.700</td>
<td>1.260</td>
<td>2.100</td>
<td>1.700</td>
<td>0.000</td>
</tr>
<tr>
<td>Range</td>
<td>1.750</td>
<td>2.190</td>
<td>1.960</td>
<td>2.450</td>
<td>3.400</td>
</tr>
<tr>
<td>Skewness</td>
<td>-0.963</td>
<td>-0.934</td>
<td>-0.623</td>
<td>-0.535</td>
<td>-1.093</td>
</tr>
<tr>
<td>Kurtosis</td>
<td>0.720</td>
<td>-0.696</td>
<td>0.922</td>
<td>-0.407</td>
<td>-0.914</td>
</tr>
</tbody>
</table>

of a problem, but recently a number of producers have encountered contamination with mycoplasmas. Some of these contaminations are due to the use of inappropriate techniques and practices, but several vaccine producers in Africa still lack the provisions or commitment to implement the basic aspects of GMP. In the absence of correct operation of a cell bank on the basis of a seed lot system, the introduction and increasing use of the Vero cell-line in rinderpest vaccine production has significantly contributed to the increase in mycoplasma contamination (unpublished findings). Another main source of mycoplasma contamination was identified as virus seed acquired by the production laboratories from various sources without quality certification, used without performing the standard quality control tests.

PANVAC has also detected BVD virus in one batch of rinderpest vaccine from an African producer and one batch from an Indian producer. In one country in East Africa, a BVD outbreak which possibly had some association with rinderpest vaccine or vaccination caused a public outcry, primarily due to the fear of rinderpest. Work conducted by the authors, with the Ethiopian National Veterinary Institute, demonstrated that 20% of calf kidneys intended for use in vaccine production were unsuitable for vaccine production due to BVD virus contamination. This was yet another reason for recommending the use of Vero cells for the production of rinderpest vaccine, as these cells are non-permissive to BVD virus.

As PANVAC has consolidated its programme, the range of quality control testing has expanded. Inevitably, during the latter phase, this has resulted in the rejection of some vaccines which would have been released at the beginning of the programme; but vaccine which passes current PANVAC testing is indeed of high quality. For example, most of the vaccine which passes PANVAC quality control tests attains a potency level three to ten times higher than the OIE minimum requirement. This is in sharp contrast to the situation at the beginning of the programme when only a minority of tested vaccine batches satisfied the OIE requirement.
**TABLE III**

Statistical analysis of the potency results of rinderpest vaccine which passed PANVAC quality control testing for each producer in Africa

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MB-8</th>
<th>A-8</th>
<th>H-4</th>
<th>M-8</th>
<th>DAM-5</th>
<th>T-4</th>
<th>K-5</th>
<th>B-7</th>
<th>D-7</th>
<th>N-5</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of batches submitted</td>
<td>96</td>
<td>18</td>
<td>27</td>
<td>41</td>
<td>164</td>
<td>94</td>
<td>14</td>
<td>9</td>
<td>7</td>
<td>38</td>
</tr>
<tr>
<td>No. of batches passed</td>
<td>93</td>
<td>14</td>
<td>11</td>
<td>28</td>
<td>94</td>
<td>69</td>
<td>9</td>
<td>5</td>
<td>6</td>
<td>24</td>
</tr>
<tr>
<td>Mean log$_{10}$ titre per dose</td>
<td>3.574</td>
<td>3.487</td>
<td>2.975</td>
<td>3.240</td>
<td>3.313</td>
<td>3.052</td>
<td>3.409</td>
<td>2.854</td>
<td>3.470</td>
<td>2.604</td>
</tr>
<tr>
<td>Standard error of mean</td>
<td>0.040</td>
<td>0.085</td>
<td>0.107</td>
<td>0.091</td>
<td>0.058</td>
<td>0.056</td>
<td>0.158</td>
<td>0.077</td>
<td>0.237</td>
<td>0.058</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>0.388</td>
<td>0.319</td>
<td>0.357</td>
<td>0.484</td>
<td>0.561</td>
<td>0.464</td>
<td>0.475</td>
<td>0.172</td>
<td>0.579</td>
<td>0.287</td>
</tr>
</tbody>
</table>

PANVAC: Pan-African Veterinary Vaccine Centre
TABLE IV

**Statistical analysis of the potency results of combined rinderpest/contagious bovine pleuropneumonia vaccine which passed PANVAC quality control testing for each producer in Africa**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Laboratory code</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A-8</td>
</tr>
<tr>
<td>No. of batches submitted</td>
<td>34</td>
</tr>
<tr>
<td>No. of batches passed</td>
<td>32</td>
</tr>
<tr>
<td>Mean (\log_{10}) titre per dose</td>
<td>3.735</td>
</tr>
<tr>
<td>Standard error of mean</td>
<td>0.070</td>
</tr>
<tr>
<td>Median</td>
<td>3.815</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>0.397</td>
</tr>
</tbody>
</table>

PANVAC: Pan-African Veterinary Vaccine Centre

TABLE V

**Causes of quality control failure of rinderpest vaccines in Africa from 1988 to June 1994**

<table>
<thead>
<tr>
<th>Year of submission</th>
<th>No. of batches tested</th>
<th>No. (%) of batches failed</th>
<th>Potency</th>
<th>Sterility</th>
<th>Mycoplasma</th>
<th>Adventitious viruses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1988</td>
<td>86</td>
<td>33 (38.4%)</td>
<td>33 (38.4%)</td>
<td>2 (2.32%)</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>1989</td>
<td>86</td>
<td>38 (44.2%)</td>
<td>27 (31.4%)</td>
<td>28 (32.5%)</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>1990</td>
<td>107</td>
<td>36 (33.6%)</td>
<td>24 (23.2%)</td>
<td>20 (18.7%)</td>
<td>ND</td>
<td>0</td>
</tr>
<tr>
<td>1991</td>
<td>111</td>
<td>32 (28.8%)</td>
<td>28 (25.2%)</td>
<td>15 (13.5%)</td>
<td>ND</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>1992</td>
<td>125</td>
<td>13 (10.4%)</td>
<td>5 (4.0%)</td>
<td>8 (6.4%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1993</td>
<td>144</td>
<td>62 (43.0%)</td>
<td>34 (23.6%)</td>
<td>13 (9.0%)</td>
<td>31 (21.5%)</td>
<td>1 (0.7%)</td>
</tr>
<tr>
<td>1994 **</td>
<td>35</td>
<td>12 (34.3%)</td>
<td>1 (2.8%)</td>
<td>5 (14.3%)</td>
<td>7 (20.0%)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>694</td>
<td>226 (32.6%)</td>
<td>152 (29.9%)</td>
<td>91 (13.1%)</td>
<td>38 (5.5%)</td>
<td>2 (0.29%)</td>
</tr>
</tbody>
</table>

ND: no data

* vaccine received from South Asia

** year to June

CONCLUSIONS AND LESSONS

This presentation has concentrated on the impact of standardised quality control testing on the quality of a vaccine used in a regional disease control campaign. This has been illustrated through consideration of the work of PANVAC on rinderpest vaccine in Africa. The impact of PANVAC has not been restricted to a filtering mechanism to ensure that vaccine lots released for the campaign meet the minimum requirement; PANVAC has also been active in the improvement of vaccine quality at the producer level. A similar trend in vaccine quality improvement has been demonstrated for CBPP vaccine (14, 9). In South America, a remarkable improvement in foot and mouth disease vaccine quality was observed following the standardisation of methods and criteria designed by the Pan American Foot and Mouth Disease Centre (PANAFTOSA), an institution of independent national quality control testing in major...
Experience from South America and Africa shows clearly that, in developing countries, it is not sufficient to rely on voluntary adherence to the minimum requirements of the OIE or a pharmacopoeia. Independent and secondary-level quality control testing – employing test procedures which have been standardised in the region by an independent (preferably regional) institution – are pre-requisites for minimising the risk of poor-quality or potentially unsafe vaccines being widely used.

In Africa, some production laboratories were initially reluctant to co-operate with the PANVAC scheme. This was probably due to considerations of national sovereignty, institutional pride, a perception of interference by one development project in the activities of another (in countries with bilateral technical assistance projects related to vaccine production or use) and, perhaps, lack of adequate appreciation of the benefits of the scheme. This was complicated by the fact that most vaccine producers were government laboratories. In South America, similar resistance was initially encountered within the industry, which perceived government controls as excessive, likely to result in a reduction in profitability, and hence as discouraging investment. Ironically, on both continents, once the newly-established control units (PANVAC in Africa and the national units in South America) had started yielding results from which trends of improved quality were evident, manufacturers achieving good results in the tests began to use independent certification as evidence of the superiority of their product. The leading producers became champions of quality and independent testing and, in some cases, advocated checks of certain manufacturing procedures which were potentially risky. Thus, for example, Brazil was able to ban the use of formalin as the sole inactivant for foot and mouth disease vaccine when this method was still being used by certain manufacturers in Europe. Formalin inactivation is a non-linear reaction, and formalin-inactivated vaccines carry a higher risk of residual infective virus than vaccines inactivated with first-order kinetic inactivants, such as aziridine compounds (2, 4).

In South America, a regulatory base exists – at least for major vaccines. This base can be further developed to take into account improved attitudes towards quality assurance and GMP, as well as risk monitoring. Despite the eminent success of PANVAC, however, few countries in Africa have an effective regulatory system for licensing biological products and for monitoring their quality and safety. In Asia, many countries have a legal framework but no realistic system for monitoring quality or for risk assessment.

Experience from both South America and Africa shows the value of a regional laboratory in providing independent verification of methods and criteria for testing, and even actual testing of vaccines which are to be widely used in a region. In Africa, this role has been played in a modest manner by PANVAC, and in South America PANAFTOSA has been a shining example. To date, however, PANVAC is lacking a legal framework; it has been a development project with a finite life-span. Mechanisms need to be developed within Africa to ensure the financial sustainability of PANVAC, and to provide a legal framework which would enable PANVAC to exercise a regulatory function. The proposed system of charging a fee for quality control services should assist this process, provided that national Veterinary Services establish licensing mechanisms which require PANVAC certification of vaccine quality. Another contributing factor will be that governments should disengage from vaccine production, transferring these activities to the commercial sector. In this manner, government agencies are likely to place a higher value on the role of PANVAC in quality assurance and the monitoring of licensing regulations, which would be regionally harmonised.
Résulté : Les vaccins vétérinaires sont considérés comme des médicaments, et en tant que tels ils sont soumis à une évaluation pour la gestion des risques liés à leur commercialisation et à leur utilisation. Les procédures d’évaluation des risques actuellement utilisées en Afrique reposent sur des méthodes de contrôle de qualité normalisées par le Centre panafricain pour les vaccins vétérinaires (Pan-African Veterinary Vaccine Centre : PANVAC).

Les auteurs examinent les procédures d’évaluation des risques liés à l’importation de produits et à la libération dans l’environnement de produits contenant des organismes vivants. Le manque d’infrastructures, de personnel spécialisé et de ressources financières empêche chaque pays de se doter de son propre système de gestion des risques liés à l’importation des vaccins vétérinaires. Aussi les auteurs recommandent-ils une coopération régionale entre les pays de ce continent, basée sur le réseau déjà existant du PANVAC pour les contrôles de qualité des vaccins prioritaires. Le PANVAC a, en effet, à son actif notamment la normalisation des technologies de production des vaccins contre la peste bovine et la péripneumonie contagieuse bovine.

Les auteurs recommandent que le PANVAC soit utilisé pour aider la coopération régionale en Afrique à gérer les risques liés à la commercialisation et à l’utilisation des vaccins vétérinaires.

estandarización de las tecnologías de fabricación de las vacunas contra la peste bovina y la perineumonía contagiosa bovina.

Los autores aconsejan que el PANVAC sea utilizado para potenciar la cooperación regional en África en lo que concierne al manejo de los riesgos asociados a la comercialización y empleo de las vacunas veterinarias.


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REFERENCES


