LEGS

Livestock Emergency Guidelines and Standards

The Quality of Veterinary Pharmaceuticals

A Discussion Paper for the Livestock Emergency Guidelines and Standards (LEGS)

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CONTENTS

ABBREVIATIONS

AHSP	Animal Health Service Provider
AMR	Antimicrobial Resistance
CBAHS	Community Based Animal Health System
CAHW	Community Based Animal Health Worker
ECHO	European Civil Protection and Humanitarian Aid Operations
FAO	Food and Agriculture Organization of the United Nations
FMD	Foot and Mouth Disease
LEGS	Livestock Emergency Guidelines and Standards
M&E	Monitoring and Evaluation
OIE	World Organisation for Animal Health
RUMA	Responsible Use of Medicines in Agriculture Alliance
PVP	Private Veterinary Pharmacy
PVS	Performance of Veterinary Services (OIE Tool)
USAID/OFDA	United States Agency for International Development/ Office of U.S Foreign Disaster Assistance (now the USAID Bureau for Humanitarian Assistance)
VSF	Vétérinaires Sans Frontières
WHO	World Health Organisation

INTRODUCTION

The objective of this discussion paper is to inform the LEGS Technical Advisory Committee on issues relating to the quality of veterinary pharmaceuticals for livestock responses in emergency situations. This includes the elements of the supply chain as well as the pharmaceuticals themselves, and also growing concerns about how antibiotic and anthelminthic pharmaceuticals are used (and misused) in the context of the global problem of anti-microbial resistance (AMR). This Discussion Paper draws heavily on the experiences and conclusions of the LEGS Operational Research Project on "Operational barriers to applying LEGS", a review of existing literature, and interviews with key informants from agencies working within this sector (Vétérinaires Sans Frontières - VSF, Food and Agriculture Organisation - FAO, The Brooke, University/Research Institutions, LEGS trainers). The paper is structured in two sections, the first focusing on ensuring the quality of veterinary pharmaceuticals and their supply chain in an emergency, and the second on the development of anti-microbial resistance and strategies for minimizing these risks. The Annex provides case studies from Zimbabwe, Somalia and Kenya, and Niger.

1. Quality of Pharmaceuticals: inherent quality of the pharmaceuticals and the supply chain

The LEGS Operational Research Project conducted an online survey of practitioners and policy makers around the world amongst which 41% identified "ensuring quality of veterinary medicines" as a challenge (see Vetwork 2019, LEGS 2020a and LEGS 2020b). Indeed the International Federation of Animal Health has estimated the illegal veterinary medicines trade to be worth 1 billion USD annually, roughly 3% the value of the legal veterinary market (IFAH 2017). These counterfeit and unregistered products often contain lower concentrations of active ingredient (in some cases none at all), they might contain other ingredients; furthermore they may not be sterile or present other quality challenges such as being passed their expiry date. This poses a serious threat to animal health and welfare: not only may they be ineffective at treating illnesses, they could also be harmful. Furthermore with regards to human health the use of such pharmaceuticals in food producing animals can decrease food safety. Their poor efficacy also increases the risk of zoonotic diseases and the development of antimicrobial resistance (administration of below therapeutic concentration levels). Thus the illegal veterinary market not only poses a risk to animal health and welfare but also human health[1]. The scale of the problem is greater in developing countries with the trade in sub-standard and non-registered pharmaceuticals in Africa estimated to be the same size as that of the official market[2]. A number of studies on veterinary medicines in West Africa found circulating rates of sub-standard medicines to be between 43% (in Mali) and 69% (in Cameroun for oxytetracycline) (Dognon et al 2018).

1 https://healthforanimals.org/169-new-report-illegal-veterinary-medicines-impact-and-effective-control.html

2 http://www.fao.org/news/story/en/item/123165/icode/

LEGS promotes a livelihoods-based approach. The use of poor quality pharmaceuticals directly undermines livestock keepers' assets by putting the health of their key assets (livestock) at risk. The use of poor quality pharmaceuticals can result in treatment failure, adverse reactions and AMR, all leading to increased morbidity and mortality. Furthermore it can erode public confidence in Community Based Animal Health Systems (CBAHS) – a well-trained and informed animal health service provider (AHSP) will not be able to successfully treat an animal if the pharmaceuticals used are themselves deficient. Ultimately, poor quality pharmaceuticals can provide a food safety, human health and environmental risk.

This section will address the issue of quality by first of all (i) presenting the concept of quality in the context of veterinary pharmaceuticals, (ii) briefly reviewing different donor policies with regards to the procurement of veterinary pharmaceuticals, and finally (iii) proposing a framework to assist implementing agencies in ensuring the quality of veterinary pharmaceuticals within an emergency livestock response.

1.1 Definition of quality

When it comes to looking at the quality of veterinary pharmaceuticals one has to look at both the quality of the pharmaceutical and the quality of the supply chain which delivers the pharmaceutical used for treatment. The quality of a drug encompasses three elements:

- the **quality of the drug** itself: including the quality of the active ingredients and the excipient, as well as the correct concentration of the ingredients and maintenance of sterility;

- the **quality of the packaging**: does the physical packaging maintain sterility, sufficiently protect the content, and provide a clear way of identifying if integrity of packaging has been maintained;

- the **quality of the labelling**: this is important for traceability and management of stock. Labelling should clearly indicate the active ingredient and its concentration, batch number, date of production and expiry date.

Quality throughout the supply chain is essential to ensure that the quality of the pharmaceuticals is maintained from the manufacturer through to the end point of administration. Furthermore these quality standards also help prevent counterfeit pharmaceuticals from entering into the legal supply chain. It therefore covers correct storage and distribution practices from the manufacturer to the wholesaler, the private veterinary pharmacy (PVP) and to the AHSP. This includes four main elements: (i) physical storage and transport conditions: clean, temperature and moisture control, protection from vermin, restricted access etc., (ii) stock management practices: first expired first out system, stock management practices with regular inventories and clear record keeping, etc., (iii) qualified personnel and regular training, (iv) standard operating procedures and conformity with recognized certification standards.

Quality throughout the supply chain includes two further aspects. Firstly, it should cover the disposal of pharmaceuticals as improper disposal may be hazardous as it can lead to contamination of water supplies damaging aquatic life or contaminating drinking water. Furthermore, usage of products past their expiry dates could contribute to the development of AMR, have no positive effect on treatment outcome or lead to adverse reactions. Secondly it should also provide for pharmacovigilance which involves mechanisms to report upwards the adverse effects of medicines. In the context of high risks of counterfeit pharmaceuticals entering the supply chain, this upwards monitoring can also be useful for end users to report back to PVPs and wholesalers if a certain batch or drug was ineffective.

An overarching pre-requisite for maintaining the quality of the supply chain is the regulatory framework of the country and the effectiveness of its enforcement. The regulatory framework determines which pharmaceuticals are licensed for use - in which species and for which condition. Licensing decisions take into account pharmaceuticals' properties with respect to human food safety (both toxicology of drug residues and also AMR potential), animal and user safety, as well as their effectiveness. The assessment of effectiveness goes beyond the pure effectiveness of the chemical in laboratory conditions but also covers the conditions of in field treatment – for example, for areas with high temperature variation and no cold chain, licensing of medication should take into account the need to withstand high temperature ranges. The final element to be taken into consideration with regards to licensing of a particular pharmaceutical is the environmental impact of its manufacturing and disposal. For example widespread use of diclofenac in cattle in south Asia led to a severe decline in vulture populations as a result of kidney failure due to consumption of carcasses containing diclofenac. [3] Countries on the Indian subcontinent began banning diclofenac in 2006 and since then, vulture populations in the region have started to recover.

Regulatory frameworks also cover requirements with regards to manufacturing, importing, selling, prescribing and administration of different classes of pharmaceuticals. A key element are the post-market monitoring mechanisms in order to ensure compliance throughout the supply chain (quality of veterinary pharmaceuticals, compliance of pharmacies with regulations, tests for veterinary drug residues in food etc.), as well as to monitor for adverse reactions and potential development of AMR in foodborne micro-organisms. Monitoring needs to be combined with solid legal dispositions for enforcement (enabling imposition of penalties, sanctions and other methods) in order to have an effect on compliance. Whilst regulatory frameworks vary among and within regions, the key issue is the level of effective implementation which is dependent to a large extent on sufficient funding for regulatory bodies[4].

The quality of pharmaceuticals can be assessed technically with laboratory analysis of samples, and also empirically, by assessing the effectiveness of a given treatment. Indeed research with Fulani herders in Nigeria shows that they are not only aware of the problem of poor quality veterinary pharmaceuticals but have also adapted "innovative strategies to mitigate the financial and health risks involved" (Kingsley 2015). Ineffective treatments for trypanosomiasis were a major issue for these herders and they had adopted the practice of testing a drug on a small number of sick animals first and then waiting to see its result before buying more of the same product. Thus end users can assess the quality of veterinary pharmaceuticals by judging the response to treatment – which implies they can also be included in monitoring systems providing upwards feedback. However, assessing the response to treatment also relies on correct diagnosis, drug handling and administration. Ensuring the delivery of quality of pharmaceuticals is not sufficient for positive outcomes. It must go hand in hand with effective capacity building of frontline animal health services.

3 https://www.nature.com/news/cattle-drug-threatens-thousands-of-vultures-1.19839

4 Regulatory issues in exporting countries are not covered in this paper

1.2 Donor policy for quality of veterinary pharmaceuticals

In this section the policy frameworks of the European Civil Protection and Humanitarian Aid Operations (ECHO), the United States Agency for International Development/ Office of U.S Foreign Disaster Assistance (USAID/OFDA) and the Belgian Development Agency will be reviewed.

ECHO's *Review of Quality Assurance Mechanisms for Medicines and Medical Supplies in Humanitarian Aid (European Commission 2006)*[5] provides an interesting framework for understanding quality aspects throughout the cycle of the provision of human pharmaceuticals focusing on four processes:

Selection	Reviewing the prevalent health problems, identifying treatments of choice, choosing individually needed medicines and dosage forms, quantifying the medicine requirements, and deciding which medicines will be made available at each level of the health care system
Procurement	Selecting procurement methods, managing tenders, establishing contractual terms with providers, assuring drug quality, obtaining the best possible price/quality rations, and ensuring adherence to contractual terms
Distribution	Clearing customs, control of stocks, store management, and delivery to pharmaceuticals depots and health facilities
Rational Use	Diagnosing, prescribing, dispensing, and proper consumption of medicines by the patient. Waste disposal is also included in this step

The issue of selection of pharmaceuticals is important with regards to ensuring quality: pharmaceuticals should be selected which are suitable to the end user environment (storage conditions, familiarity of health professionals with the medicine, and administration skills...). This selection occurs at two levels - by the regulatory framework (which pharmaceuticals are authorized for import/manufacturing and usage) and the project (which pharmaceuticals should be procured). Selection of pharmaceuticals should take into account both the needs and ability of the health service – mass procurement of antibiotics which do not respond to a precise animal health need or end up incorrectly administered (due to lack of ability) could contribute to the development of AMR. The review highlights clear weaknesses in this area with only 52% of ECHO partners actually assessing the needs before initiating procurement.

Overall ECHO provides clear guidelines for the procurement of human medical supplies (European Commission 2011) with the procurement either from pre-certified suppliers according to World Health Organisation (WHO) minimum quality standards or from Humanitarian Procurement Centres. However the provisions for veterinary medical supplies are very scant, summarized only in two paragraphs: "the procurement of veterinary medicines, while not subject to the same quality requirements of the medical supplies, shall nonetheless be procured by the partner with due respect of the applicable best veterinary practices in the field, and where possible, in consultation with an appropriately qualified animal health expert." This leaves a lot of room for interpretation. The second paragraph focuses on adequate provisions for the destruction of veterinary supplies that are recalled or expired.

5 NB. This Review refers to human pharmaceuticals however can also apply to the veterinary context.

USAID/OFDA provides a more stringent guideline for the procurement of veterinary pharmaceuticals (USAID/OFDA 2019). Pharmaceuticals have to be purchased through pre-qualified vendors audited by USAID/OFDA and found to meet internationally accepted standards for safe, effective and quality pharmaceuticals. Currently there is one USAID/OFDA prequalified veterinary pharmaceutical vendor. Alternatively, non-prequalified vendors can be used but this requires a vetting process with a number of documents to be submitted to USAID/OFDA (Standard Operating Procedures - SOPS, organizational chart of vendor, government documents authorizing sale of pharmaceuticals, availability of certificates of analysis, computerized invoices and packing lists, assurance of expiration policy, and photographs of interior storage areas etc.).

Only pharmaceuticals listed on the OFDA Veterinary Essential Medicines List can be procured. Furthermore for every procurement activity a request must be submitted to USAID/OFDA which not only covers the vendor, type of pharmaceutical (including strength and dosage) and reason for use (species of animal and condition) and quantity to be procured but also an assurance that the partner is following all host nation policies for importation of pharmaceuticals and that it is authorized. These elements provide clear safeguards for the quality of veterinary pharmaceuticals.

The USAID/OFDA guidelines highlight that the process to approve a non-prequalified vendor can "take weeks or months depending on the information that is provided". This is a serious hurdle for an emergency response – however with regards to recurrent emergencies such as drought, under LEGS Core Standard 2 on Preparedness, LEGS encourages implementers to be ready for an emergency thus agencies could take the following steps to enable a swift response during an emergency:

- work with their vendors prior to an emergency to meet with and inspect the vendor to ensure it is compliant with OFDA quality standards and requirements

- ensure that the vendor is familiar with all paperwork necessary for approval by OFDA, and can provide the paperwork immediately once a disaster occurs so that the partner does not experience a delay in obtaining complete, acceptable paperwork.

The LEGS Operational Research report confirmed this challenge, with delay in the Ethiopia project test in part due to the time it took to get the wholesaler approved, as their initial standards were very low and required significant upgrading for their storage and stock management procedures before they could be approved by USAID/OFDA. However, it is also recognized that the approval process in itself is a form of capacity building, with the wholesaler from Jijiga confirming that *"We have an improved storage now as a result of this research. We also make quality assurance – the pharmaceuticals need a chemical name and a generic name which together with registration and route of importation ensures they are legal. In short these are the benefits from this project…we now have a good opportunity for those of us involved in trade to act as a quality wholesaler for the region."* (LEGS 2019b) Furthermore the operational research confirmed it was possible to apply OFDA guidelines to an emergency context using a voucher scheme for the procurement of quality pharmaceuticals through the local supply chain.

The Belgian Development Cooperation's guidelines are set out in its *"Engagement pour une assurance de la qualité des produits pharmaceutiques"* (2017) which is co-signed by all its implementing partners including Vétérinaires sans Frontières Belgium. This document includes two elements not covered by USAID/OFDA:

(i) A commitment to strengthening the local capacities of the supply chain in partner countries in order to guarantee the quality of pharmaceuticals

(ii) A commitment to guaranteeing the quality of pharmaceuticals purchased and distributed through the establishment of a monitoring and evaluation (M&E) system.

Quality assurance (QA) is a key concern and it stipulates that the costs for QA of pharmaceutical products are explicitly included in the project budget. QA encompasses:

- Pre-qualification of vendors, and monitoring and evaluation;
- Risk Analysis and Risk Management Plan which should include SOPs;
- M&E of pharmaceuticals including spot check laboratory testing of pharmaceuticals.

These guidelines set out the core principles for action: procurement where possible within local supply chains, capacity building of local supply chains and clear QA procedures including testing. However, compared with the USAID/OFDA guidelines they are not very specific with regards to the "how", mostly deferring to WHO standards.

The commitment to strengthening local supply chains mirrors LEGS policy to support local markets. Core Standard 4: Initial assessment and response identification - Guidance note 3 states that "interventions that support local services and markets are an important aspect of livelihoods-based programming". Multiple sources (LEGS Operational Research Report, Country Performance of Veterinary Services (PVS) reports, interviews with key informants) all highlight the challenges that the emerging private veterinary sector faces with the competition induced by the provision of free pharmaceuticals by projects and government interventions and due to the high prevalence of cheap illegal pharmaceuticals. Emergency interventions should aim to build existing capacity - and thus the local veterinary private sector including its supply chain.

Therefore with regards to veterinary drug procurement, it is strongly recommended to procure through existing legal local supply chains - in many cases this will go hand in hand with capacity building of the local supply chain in order to ensure the quality of the pharmaceuticals. The implementing agency should procure and import directly only in cases where the supply chain has broken down due to conflict or an acute extreme emergency. In those cases it is still recommendable to procure within the sub-region where possible so as to strengthen regional markets. Such approaches often will also enable a more timely procurement.

The below table summarizes the pros and cons of different procurement options.

	Advantages	Disadvantages
Procurement by project internationally with direct distribution to CAHW	Pharmaceuticals may be of high quality depending on country of origin Good oversight of distribution conditions Good option where no local legal supply chain	Creates competition with and can undermine local supply chain Doesn't create sustainable linkages for CAHWs to re-stock with medicines and for safe disposal Transport to insecure areas can pose a challenge Potential delays / slower procurement
Procurement by project locally from approved wholesaler or PVP with direct distribution from project to CAHW	Timeliness of delivery (especially if pre-registered) Certain quality standards can be upheld such as expiry dates Supports local supply chain	Requires more stringent M&E in order to ensure quality of pharmaceuticals Pre-registration of supplier can in some cases lead to delays if low initial standards Doesn't create sustainable linkages for CAHWs to re-stock with medicines and for safe disposal Small risk of lower quality pharmaceuticals entering supply chain Not recommended where local capacity is too weak to meet minimum standards
Procurement via voucher mechanism linking approved CAHW with PVP (+/- Wholesaler)	Timeliness of delivery (especially if pre-registered) Certain quality standards can be upheld such as expiry dates Strengthens local supply chain Creates sustainable linkages between CAHW and PVP Pharmaceuticals procured on a needs basis - less risk of wastage	Requires more stringent M&E in order to ensure quality of pharmaceuticals Can take longer to set up (pre-registration, MoU between actors…) Small risk of lower quality pharmaceuticals entering supply chain – however direct CAHW/ livestock herder feedback mechanism possible
Procurement by project locally using whatever suppliers / medicines available (no pre-registration or QA)	Timeliness	No quality assurance with regards to appropriate storage, traceability etc. Higher risk of lower quality and counterfeit pharmaceuticals: poorer treatment outcomes and risk of contributing to resistance Doesn't create sustainable linkages for CAHWs to re-stock with medicines and for safe disposal

1.3 Framework for ensuring quality of veterinary pharmaceuticals

Drawing on the findings from the literature review and interviews with key informants, the following framework is proposed for ensuring the quality of veterinary pharmaceuticals procured in an emergency livestock context.

The framework is based on 7 key steps – the majority of which should be applied during the preparedness phase:

Step 1	Participatory Mapping of the Supply Chain and Regulatory Framework Analysis

Participatory mapping of the supply chain providing an overview of all actors and the flows of pharmaceuticals within both the formal and informal supply chain landscape. It should also cover:

- Level of quality standards of each actor with regards to procurement, storage and distribution
- The decision basis underlying the commercial linkages: actors may choose to purchase from a particular wholesaler/PVP because of convenience distance-wise, trust, reliability of the pharmaceuticals, credit options, preferred type and packaging of pharmaceuticals provided
- Regulatory framework analysis is important for understanding which pharmaceuticals are registered for use in the country and who is allowed to manufacture, import, prescribe, sell and administer pharmaceuticals and which QA mechanisms exist and their level of enforcement

Step 2	Pre-selection of Supply Chain Partners and Selection of Pharmaceuticals

Drawing from OFDA's guidelines and the operational research's findings, it is recommended that LEGS establish a simplified guideline with differentiated standard levels for the storage and distribution of pharmaceuticals (basic, medium, advanced) based on the context of the wholesaler and also the medicines they supply. This guideline should serve for pre-qualifying wholesalers prior to emergencies. Separate standards should be established for PVPs and AHSPs.

The authorized list of pharmaceuticals should respond to the needs of the particular livestock emergency and take into account the storage and distribution environment (ambient temperatures, presence of cold chain, need for long acting medicines…) as well as the local priority diseases as identified by livestock owners and local AHSPs. Furthermore it should be kept as simple as possible if relying on a CBAHS so as to safeguard drug administration quality.

Pre-selection of supply chain partners and choice of pharmaceuticals go hand in hand:

- If a list of "simple" pharmaceuticals (topical/oral, stable over a wide temperature range for example) is chosen then a "basic standard" supplier may be sufficient and conversely if the supply chain cannot guarantee the cold chain, it is inadvisable that temperature sensitive vaccines, for example, be included in the approved pharmaceuticals list
- Supply chain actors may have detailed knowledge with regards to the current disease situation in the area, preferred treatment methods and end user needs in order to better inform the decision on type of pharmaceuticals to be selected (for example with respect to Newcastle Vaccine administration route: if the end-user has a typical herd size of 5 chickens administration with eye drops is acceptable, if herd size is 100 they may prefer administration through drinking water)

Step 3	MoU among Supply Chain Actors (Wholesaler, PVP, AHSP)

If the procurement process is to follow a voucher scheme or engage multiple levels of the supply chain (as opposed to procurement by the project directly from a wholesaler) then a Memorandum of Understanding is key for building trust among supply chain actors and establishing a transparent process. The project only plays the role of facilitator in getting all actors to sit at the same table and for them to discuss and negotiate with each other. The MoU clarifies the process with regards to payment terms and sets the prices negotiated and agreed between supply chain actors.

Furthermore, it is an opportunity for knowledge sharing: PVPs may better understand end-user needs and demand, a wholesaler may be able to provide advice on storage, together transport and timing issues may be overcome. Also it helps bring everyone up to the same knowledge level - if a project is advising livestock herders to only administer oral or topical medicines themselves, then it is important for the PVPs to also know this to make sure they stock the oral/topical medication and also promote the same advice to livestock herders (see Pakistan case-study).

The MoU should define some elements of the M&E system including feedback between the actors and for safe disposal of waste pharmaceuticals.

The linkage between PVP and AHSPs is especially important in order to ensure on the one hand capacity building and monitoring, and on the other hand to secure the supply of quality pharmaceuticals (See Niger case study).

Step 4	Capacity Building of Supply Chain Actors (Wholesalers, PVPs, AHSPs)

Capacity Building should be:

- Based on a needs assessment and tailored to the needs of the actor. in some cases, no capacity building may be needed (for example the LEGS Operational Research Project found high standards among wholesalers in Zimbabwe)
- Training measures could include also non pre-qualified suppliers in order to improve their standards and the public sector in order to support their capacity to enforce their regulatory role (see Somalia case study)
- Both training and mentoring based - as mentoring in the workplace has been shown to be important for helping actors to apply the knowledge to their setting

Step 5	Awareness Raising Within The Community

Training-based strategies can enable livestock herders to make more informed decisions with regards to pharmaceutical quality:

- Training needs assessment so that training responds to specific knowledge gaps/practice
- Choosing treatment through a trained AHSP who provides reliable quality pharmaceuticals
- Understanding the risks of poor quality and counterfeit pharmaceuticals as well as understanding how to identify and report them
- Understanding correct administration, withdrawal periods, and safe disposal of pharmaceuticals they are legally allowed to purchase and administer themselves

Step 6	Monitoring and Evaluation

M&E is a central pillar for quality assurance and should take into account the following aspects:

- Multilevel throughout supply chain: wholesaler, PVP, AHSPs
- Multiple methods: monitoring of traceability throughout the supply chain, spot checks, and user feedback (community and AHSP) with regards to effectiveness should be the mainstay for any M&E system. Where doubts are raised with regards to the quality of a particular batch of medicine, they should be sampled and tested for the quantity of active ingredient and microbial load with respect to product sterility. Standard sampling and testing as conducted during the operational research can be too costly and time-intensive and therefore not recommended on a regular basis. However, where doubts are raised it is an effective last level check
- Actors involved in M&E: project, livestock herders, state technical services, PVPs
- Mechanism for upwards feedback: adverse drug reaction, ineffective drug or suspected counterfeit

The regulatory framework of the country will inform the design of the M&E system. If the country has a strong regulatory system testing imported and locally manufactured pharmaceuticals and also spot checks throughout the distribution network, then the M&E of the project might not need to be as stringent.

Step 7	Strengthening the Regulatory Framework & Enforcement

In the long term and under emergency preparedness there is a need to work closely with government agencies responsible for setting quality standards to ensure that they are appropriate for the end-use environments including:

- Regulation and licensing of private veterinary pharmacies, wholesalers, local manufacturers and importers
- Regulation of pharmaceuticals and quality standards: for example, it is important to ensure that standards for licensed pharmaceuticals (imported or locally manufactured) regarding temperature and stability are appropriate for the environment where the pharmaceuticals will be used

The majority of the elements under this framework clearly fit under preparedness planning (LEGS Core Standard 2). Having these systems in place before an emergency will enable a more rapid response whilst ensuring quality. Community involvement is important at multiple stages throughout the framework: with regards to mapping supply chain, informing drug selection, capacity building and M&E. The above framework for veterinary pharmaceuticals can also be extended to cover veterinary equipment. With regards to disposal, particular attention needs to be given to the challenge of disposal of needles and scalpel blades.

2. Antimicrobial Resistance

Anti-microbial resistance refers to micro-organisms – bacterial, fungi, viruses, and parasites – that have acquired resistance to antimicrobial substances. Whilst this phenomenon occurs naturally through microbial adaption to the environment, it is exacerbated and accelerated through the inappropriate and excessive use of antimicrobials.

2.1 Problem of Antimicrobial Resistance

Various underlying factors contribute to the development of AMR: i) lack of regulation and oversight of use ii) poor therapy adherence; iii) non-therapeutic use; iv) over-the-counter sales; and v) availability of counterfeit or poor-quality antimicrobials (FAO 2016).

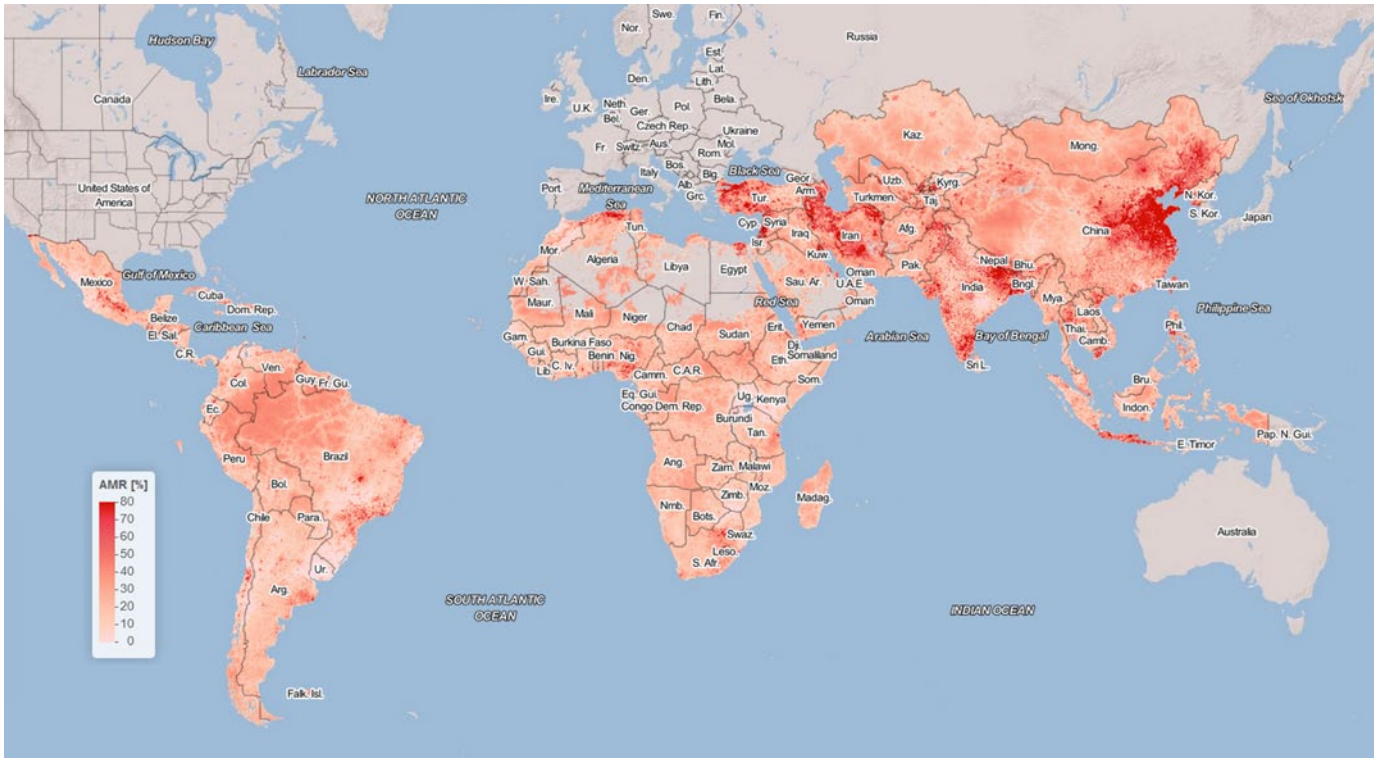
The consequences of antimicrobial resistance go beyond eroding livestock herders' key assets (due to ultimately increased morbidity and mortality among livestock) and reducing food security, but also present a risk to public health.

The World Health Organisation (WHO), FAO and the World Organisation for Animal Health (OIE) have developed a tripartite collaboration on Antimicrobial Resistance with the development of a Global Action Plan. As key leaders on this topic, the websites of all three organizations were reviewed in order to find up to date data with regards to prevalence of AMR in livestock. WHO provides no data with regards to levels of AMR in the food chain. However it does provide a guideline on "integrated surveillance of antimicrobial resistance in foodborne bacteria. Application of a one health approach". For the human health sector it launched in 2015 a Global Antimicrobial Resistance Surveillance System (GLASS). The 2018 GLASS report covers the 69 countries enrolled in GLASS of which 26 are lower and lower-middle income countries (WHO 2018). However for the majority of the lower income countries no data was yet available as they had just joined GLASS in 2018 and are in the infancy stages of setting up their surveillance system (since then some countries such as Ethiopia have published their first set of data in 2020).

FAO and OIE both provide data on antimicrobial usage in livestock (OIE 2020). Other initiatives, such as the Livestock Antimicrobial Partnership (LAMP) under the Global Agenda for Sustainable Livestock, collects experience on best-practices. Of the 136 member countries assessed through an initial OIE Performance of Veterinary Services (PVS) Evaluation up to December 2019, almost three quarters do not regulate veterinary medicinal products. The OIE PVS has developed a new Critical Competency on Antimicrobial Resistance and Antimicrobial Use in order to address this. Currently there is very little information available worldwide on resistance patterns in animal pathogens. Thus FAO and OIE are supporting countries to develop multi-sectoral National Action Plans to address AMR using a One Health Approach as well as strengthening laboratory capacities in order to improve AMR within the food chain.

Until such surveillance systems are fully functioning the best source of data with regards to antimicrobial resistance in low and middle income countries is the mapping provided by https://resistancebank.org/ which covers 901 prevalence surveys of pathogens in developing countries in order to map resistance.

The findings are covered by Van Boeckel et al (2019). They show a significant increase of resistance to pharmaceuticals in intensive poultry and pig sectors. The largest hotspots of AMR were in Asia (in particular China and India) which is home to 56% of the world's pigs and 54% of chickens. The rapid increases in AMR in chickens and pigs compared to cattle are consistent with the intensification of livestock operations for these species compared with cattle production which is largely more extensive. This is consistent with other studies (Founou et al 2018) and suggests that AMR among LEGS target groups is likely to be lower as they are not based on intensive farming (smallholders and pastoral settings). The study also identifies central India and Kenya as hotspots for the emergence of AMR: resistance to multiple pharmaceuticals has appeared but has not yet reached 50%. Overall AMR levels are low in Africa. Meat consumption is still low however animal production is gradually intensifying. The authors



therefore identify that there may be a window of opportunity to contain AMR in these areas by imposing strict hygiene measures.

An interesting insight is that a leading factor associated with the spatial distribution of resistance was travel time to cities. This suggests that the ease of access to providers of veterinary pharmaceuticals may drive AMR - furthermore it is likely that intensive farms might be closer to the urban affluent citizens they supply.

Despite clear data on the scale of the problem in many developing countries FAO highlights that "AMR is a global problem. Resistant micro-organisms and genes do not recognize geographical or ecological borders. Resistance arising in one geographical location or species can spread with ease to other geographical locations through movements of food, water, animals and/or people; it can spill over into other species, impacting developed and developing countries alike." In line with a logic of "Do no Harm", emergency interventions dealing with livestock health and anti-microbial usage should strive to apply best practices for reducing the risk of developing antimicrobial resistance.

Figure 1: Geographic distribution of AMR hotspots in Low and middle Income Countries. The hotspots of AMR represent the proportion of antimicrobials used in each location (pixel) with resistance higher than 50% (P50) (Source Van Boeckel et al 2019)

2.2 Strategies to reduce development of AMR

Based on the tripartite agreement between OIE-FAO-WHO, both OIE and FAO have developed strategies with regards to preventing AMR which mirror each other:

	OIE Strategy on Antimicrobial Resistance and the Prudent Use of Antimicrobials	**FAO Action Plan on Antimicrobial Resistance 2016-2020**
Focus Area 1	Improve awareness and understanding	Improve awareness on antimicrobial resistance and related threats
Focus Area 2	Strengthen knowledge through surveillance and research	Evidence - develop capacity for surveillance and monitoring of antimicrobial resistance and antimicrobial use in food in agriculture
Focus Area 3	Support good governance and capacity building	Strengthen governance related to antimicrobial use and antimicrobial resistance in food and agriculture
Focus Area 4	Encourage implementation of international standards	Promote good practices in food and agriculture systems and the prudent use of antimicrobials

Furthermore RUMA (Responsible Use of Medicines in Agriculture Alliance) provides both general guidelines and guidelines per species and type of antimicrobial with regards to best practices.

Focus areas 2 (surveillance) and 3 (governance) may be beyond the scope of emergency based interventions. However, the following practices to improve awareness (focus area 1) and promote good practice (focus area 4) should be integrated into livestock emergency programming:

(i) Focus on prevention and prophylaxis: good animal husbandry (management and hygiene) and animal nutrition are key to reducing the use of antimicrobials. This involves capacity building of livestock keepers and frontline animal health services which provide extension messages. This can be complemented with vaccination against key diseases (linking in with public animal health strategies).

(ii) Rational and targeted use of antimicrobials:

- Treatment with antimicrobials should take place only after diagnosis of a condition by an animal health professional (a veterinarian or a para-veterinarian, which includes CAHWs), in line with national regulations on use of these pharmaceuticals by the different cadres of AHSPs. The linkage between veterinary para-professionals and veterinarians and state services is important with regards to identifying new disease outbreaks which require particular control strategies as opposed to antibiotic treatment (for example vaccination to control an FMD outbreak).
- Projects should refrain from blanket treatments such as mass de-worming and instead only treat sick animals, since a key element for preventing AMR is to decrease the usage of antimicrobials. Specifically with regards to anthelmintic resistance, mitigation strategies include keeping a population of non-treated (and thus non-resistant) parasites to dilute out parasites developing resistance to treatment. The best approach ultimately is to opt for targeted treatment based on case presentation and diagnosis.

(iii) Procurement of antibiotics should be justified on the basis of a needs assessment and projects should refrain from mass purchases of antibiotics. Van Boeckel et al's 2019 study highlights that ease of access to providers of veterinary pharmaceuticals may drive AMR. Hence projects should not artificially flood a region with antibiotics due to the risk of increasing AMR. In this respect voucher schemes are an intelligent design as procurement of pharmaceuticals can be decentralized on a needs basis (each individual AHSP procures directly from their PVP according to needs amongst the herds they treat, as opposed to central procurement from a project directly from a wholesaler or PVP). It is difficult for central procurement to be all knowing with regards to type and volume of pharmaceuticals needed within an emergency.

(iv) Use of quality medicines – strengthening the formal supply network via PVPs and AHSPs can improve access to quality medicines, and reduce usage of counterfeit and poor quality pharmaceuticals. Furthermore, improved availability will also reduce the likelihood of under-dosing/ sporadic use.

(v) Training-based strategies enable market participants to make more informed decisions- these should include a One Health focus:

- Education and awareness raising of AHSPs and (private and public) veterinarians with regards to AMR risks and mitigation measures

- Awareness raising campaigns at the livestock keeper level (risks of AMR, importance of good animal husbandry to reduce drug usage, treatment only after diagnosis, awareness of counterfeit low quality pharmaceuticals, and also withdrawal periods).

Conclusions

In conclusion the above-mentioned strategies for ensuring pharmaceutical quality and for reducing the development of AMR rely on the LEGS Core Standard 2: Preparedness. Core Standard 6: Monitoring and Evaluation is also key for guaranteeing the quality of pharmaceuticals provided and should be incorporated into the design of any procurement action. With regards to best practices in pharmaceuticals storage, handling and administration (including for the reduction of AMR) training at all levels is a key approach. Widespread awareness-raising is essential for combatting both the trade in counterfeit pharmaceuticals and risks of AMR. It is worth incorporating One Health approaches into such activities. Community participation at multiple stages from planning, implementation and M&E will strengthen outcomes.

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Case Studies

Impact Case Study: M&E of veterinary pharmaceutical procurement in Zimbabwe

The LEGS Research Project "Operational Barriers to Applying LEGS" looked at three partner projects in Ethiopia, Kenya and Zimbabwe using voucher schemes for the procurement of pharmaceuticals locally. The research model covered multiple elements including the monitoring system. In the case of Zimbabwe the monitoring of pharmaceuticals looked at all levels from the wholesaler, to the PVPs, CAHWs and community assessment. Methods included random inspections of storage facilities and CAHWs kits, checking both physical storage conditions and stock management, as well as distribution procedures including traceability throughout the supply chain (batch numbers for example). Laboratory testing of drug quality was done on samples taken at both PVP and CAHW level.

Spot checks confirmed high quality standards at the level of the wholesaler, however PVP spot checks revealed varying levels in quality management. CAHW spot checks established that CAHWs kept storage bags tidy and medicine had long expiry dates. Interestingly women CAHWs maintained good treatment and voucher redemption records - whereas men's records were poor. This highlights the potential benefits of gender sensitive approaches in the selection of CAHWs with respect to quality of record-keeping.

Community Assessments deemed that the availability, affordability and quality of veterinary pharmaceuticals had significantly improved during the voucher scheme. Traceability and laboratory results confirmed that all pharmaceuticals sold were the same pharmaceuticals used throughout the supply chain from the wholesalers to the CAHWs. Furthermore, the quality of pharmaceuticals with regards to quantity of active pharmaceutical ingredient as indicated on the label, remained stable throughout the supply chain and product sterility was maintained. In conclusion the development of a robust monitoring system helped contribute to assessing and thus ensuring the quality of pharmaceuticals provided through the project.

Process Case Study: Local procurement of veterinary pharmaceuticals in Somalia

The experience of Vétérinaires Sans Frontières Suisse (VSF Suisse) in the context of USAID/OFDA funded projects from 2015-2019 in Gedo Region, Somalia provides interesting insights with regards to capacity building of the local pharmaceutical supply chain. The USAID/OFDA pre-qualified wholesalers in the region did not supply veterinary pharmaceuticals. Despite the weak government within the intervention region, the private sector was found to be well organized with the "South West Livestock Professional Association SOWELPA" ensuring standards for animal health service provision including quality of pharmaceuticals. VSF Suisse therefore requested USAID/OFDA approval for an open tendering for local supply of veterinary pharmaceuticals and other medical commodities. One Kenyan supplier and four Somalian suppliers responded to the tender. The ability of the Kenyan wholesaler to deliver supplies due to security challenges was an issue. A Somalian supplier was therefore selected as it was able to meet OFDA quality requirements including: official national registration as supplier of veterinary pharmaceuticals and equipment, provision of Certificates of Drug Test Analysis for all pharmaceuticals supplied, commitment to provide pharmaceuticals with an expiry date of at least a year. Quality checks were performed by VSF to verify provided pharmaceuticals met specifications (for example expiry dates). OFDA approved the supplier for this proposal. Approval had to be sought again for subsequent proposals using the same USAID/OFDA approval process, but each subsequent proposal review process was quicker because the capacity of the vendor, and most importantly, of the partner, to provide the necessary documents improved over time. This meant that all USAID/OFDA quality requirements were met whilst reducing the duration it took to procure veterinary supplies, ensuring that emergency veterinary responses were not delayed.

continued

In addition VSF conducted training of the owners and attendants for all 11 identified private pharmacies within the intervention region, with regards to proper handling and storage of veterinary pharmaceuticals (including business skills and record keeping). This training was extended to include the emerging government veterinary services as they have a future responsibility with regards to regulation and monitoring. CAHWs as front-line providers of animal health services in remote rural areas also provide extension messages on the use of antimicrobials, including adherence to withdrawal periods for various livestock products. Thus the training of 120 CAHWs also included the care and management of veterinary pharmaceuticals. Furthermore with respect to antimicrobial resistance, a One Health approach was used to train 54 CAHWs and 66 community health workers through Training of Trainers courses on the links between human, animal and environmental health including the proper use of antimicrobials and resistance. Dialogues were also held with 387 community members for awareness raising on these topics.

VSF's experience demonstrated that:

- Procurement of quality veterinary pharmaceuticals was possible through the local supply chain
- Ex-post evaluations confirmed that pharmaceuticals were always delivered on time
- The capacity of the local supply chain was strengthened through training measures
- Mapping, pre-selection and strengthening of local suppliers of veterinary pharmaceuticals and other medical commodities should be done in order to be able to respond quickly to emergencies

Process Case Study: Niger PPVS Model – model for a quality supply chain

In Niger the model of Proximity Private Veterinary Services (PPVS) has been piloted by projects and implementing agencies such as Vétérinaires Sans Frontières Belgium (VSF-B) since 2003 and adopted by the state as a model for provision of animal health services in 2011. The model is based around a Rural Veterinary Clinic run by a private vet, and an associated network of CAHWs from the communities they serve. In addition local Agrodealers are linked to the private veterinarians and CAHWs (if the distance between vet and CAHW is large, CAHWs can resupply from the Agrodealer). Actors are linked together through Memoranda of Understanding. At the end of the project a sustainable network of animal health actors should remain, ensuring the durability of actions.

The formal linkages between the vet and CAHWs confirmed in a MoU help establish a constant and secure supply of quality medicines. Furthermore the model provides multi-level monitoring of the supply chain. CAHWs are monitored by the vets with whom they are linked through trimestral meetings and state technical services conduct twice yearly checks on their veterinary kit and records. The vets are in turn monitored by the state technical services. Herders associations can provide feedback to the project and technical state services with regards to the quality of the service provided by the PPVS.

Project support covers four key areas of action: (1) awareness raising among herders, (2) support to private vets including selection, technical, methodological and financial assistance for the establishment of the PPVS, and support to the establishment of a reliable and effective supply chain for medicines (3) support to CAHWs including selection, training (also covers pharmaceuticals storage and stock management) and coaching, and (4) strengthening legal control framework which includes training of state agents.

The 2019 PVS found that the development of the PPVS model had led to an improved coverage of the country with veterinary services enabling the vaccination of almost 70% of the national herd. Whilst free treatment by state agents and cheap counterfeit pharmaceuticals remained a challenge, the PVS clearly recommended the extension and strengthening of the PPVS model. A VSF-B assessment found that 94% of herders surveyed judged that PPVS possessed appropriate medication. Furthermore herders were satisfied with the results of the system reporting that body condition, fertility and milk yields had improved.

Process Case Study: Antimicrobial resistance prevention strategies in Pakistan

With regards to preventing the development of antimicrobial resistance The Brooke Pakistan has developed a number of strategies which revolve around developing evidence based best practice guidelines, and awareness raising among all key actors (from livestock owners, to para-professionals, vets and pharmacies). In 2015 Brooke Pakistan conducted a study covering four treatment centres (Lahore, Multan, Gujranwala and Peshawar) to assess gastrointestinal worm load (species and prevalence) and efficacy of the commonly used anthelmintics, Fenbendazole and Ivermectin. The study showed parasite load varied significantly among the centres with 83.6% of animals assessed in Peshawar having an egg count over 250 eggs per gram, as opposed to only 35.5% in Lahore. Furthermore resistance varied with Peshawar showing resistance to both Ivermectin (39%) and Fenbendazole (25%). In Lahore resistance was high to Fenbedazole (44.5%) and in Multan resistance to Ivermectin was emerging (10%). Resistance was not identified in Gujranwala.

Based on this information Brooke was able to develop an evidence-based best practice protocol for gastrointestinal parasites which recommends discontinuing traditional deworming practices consisting of blanket treatment every three months in favour of a targeted strategy which follows the following principles: (i) Provide treatment only on the basis of a clinical diagnosis (ii) Choose an appropriate anthelmintic based on resistance profile in the region (for example avoid Fenbedazole in Lahore), (iii) Do not treat again for another six months at the earliest. For effective implementation of this protocol it was essential to engage with the community in order to help them understand the problem of anthelmintic resistance and the disadvantages of inappropriate deworming as well as raise awareness on best practice.

Brooke Pakistan's awareness-raising and capacity building strategy has multiple levels focussing on veterinarians (public and private), storekeepers (vets, pharmacists, agrodealers), frontline animal health service providers and the community. In order to provide coherent messages one day workshops at district level with all actors in order to discuss best practice have been very useful. Not only do they provide an environment to discuss best practice (for each condition which drug dosage and administration route) but they also help establish a coherent approach and message throughout the supply chain. For example Brooke is sensitizing communities to use pharmaceuticals only in oral or topical forms- it is therefore important to ensure that the veterinary pharmacies also stock the oral forms and provide similar advice.

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