Rational Drug Use

To better manage trypanosomosis and trypanocide resistance

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Working Paper 4
May, 2003

INTERNATIONAL LIVESTOCK RESEARCH INSTITUTE
The project “Managing trypanocide resistance in the cotton zone of West Africa: A coordinated regional study” seeks to ensure the future efficacy of trypanocides as an effective component of improved integrated trypanosomosis control strategies in the region. To achieve this goal, national research and development institutions, international and regional research centres, and German universities are working in partnership to develop farm-level and regional strategies for reducing the risk of trypanocide resistance. The emphasis is on improving informational and technical supports to farmers, service providers, veterinary professionals and policy-makers that will promote integrated control and Rational Trypanocide Use to reduce the long-term risk of resistance, without compromising the ability of livestock keepers to protect their livestock from the debilitating effects of trypanosomosis.

The project is being implemented in Burkina Faso, Mali, and Guinea by the International Livestock Research Institute (ILRI) in collaboration with:

- Freie Universität Berlin, Germany
- University of Hannover, Germany
- Centre International de Recherche-Développement sur l’Elevage en Zone subhumide (CIRDES), Bobo-Dioulasso, Burkina Faso
- International Trypanotolerance Centre (ITC), The Gambia
- Direction Provinciale des Ressources Animales (DPRA), Burkina Faso
- Programme National de Gestion de la Terroir (PNGT), Burkina Faso
- Laboratoire Central Vétérinaire (LCV), Mali
- Institut d’Economie Rurale/Centre Régional de la Recherche Agricole Sikasso (IER/CRRA), Mali
- Unité de Lutte contre la Trypnomosose (ULCT), Mali
- Direction Nationale de l’Elevage et l’Institut de Recherche Agronomique de Guinée (DNE/IRAG), Guinea-Conakry
- Service de Lutte contre la Trypanosomiase Animale et les Vecteurs (SLTAV), Côte d’Ivoire
- Institut National Polytechnique Houmphouey Boigney (INPHB)

The three-year project, which began in March 2002, is funded by the German Federal Ministry for Economic Cooperation and Development (BMZ) and managed by GTZ (GTZ Project Number 2001.7860.8 – 001.00; Contract Number: 81052542).

This series of Working Papers is intended as a medium for presenting preliminary analysis and results being generated under the project.
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List of acronyms

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<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>DIM</td>
<td>Diminazene aceturate</td>
</tr>
<tr>
<td>FCFA</td>
<td>Community of French-speaking Africa franc (500 FCFA = US$ 1)</td>
</tr>
<tr>
<td>ISMM</td>
<td>Isometamidium chloride</td>
</tr>
<tr>
<td>KAP</td>
<td>Knowledge, Attitude and Practice survey</td>
</tr>
<tr>
<td>MR</td>
<td>Multiple Resistance</td>
</tr>
<tr>
<td>RDU</td>
<td>Rational Drug Use</td>
</tr>
<tr>
<td>TC</td>
<td>Trypanocide</td>
</tr>
<tr>
<td>USA</td>
<td>United States of America</td>
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<td>WHO</td>
<td>World Health Organization</td>
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</table>
1 Introduction: Summary and context

This report discusses how trypanosomosis and resistance to trypanocides can be better managed by promoting the rational use of trypanocides (and their alternatives) at community level. It outlines the need for rational use and the evidence that current use is irrational, and goes on to briefly review the different instruments for promoting rational drug use, using examples drawn from human health. On the basis of this, an evidence-based framework is suggested for promoting Rational Trypanocide Use, consisting of five elements: first, assessing the extent and impact of trypanosomosis and resistance; second, understanding the policy and practice of drug use; next, identifying fail points in usage patterns; on this basis, choosing strategies for improved drug use; and finally, implementing and evaluating the strategies. The report describes how this framework is being used in an intervention to improve trypanocide use in villages in Burkina Faso. An accompanying report gives details on a course on rational use of trypanocides given to farmers and local experts as part of this intervention.

The activities described here took place within the project “Improving the management of trypanocide drug resistance in the cotton zone of West Africa: A co-ordinated regional study”. This project has the overall goal of improving the livelihoods of smallholder farmers in West Africa, where trypanosomosis is a major threat to livestock and to the animal traction systems that farmers rely on for food and income. The project objective is to safeguard farmers’ options for managing trypanosomosis. It is working in three countries (Mali, Burkina Faso and Guinea) and addresses policy, practice and economic aspects of trypanosomosis control in the presence of drug resistance. In Burkina Faso, the project supports participatory, community-based control in four villages. As part of the participatory process, villagers identified strategies to better manage trypanosomosis control, and a priority choice for all villages was the improved use of trypanocides through training and information provision. In response to farmers’ demands, a programme for rational use was developed using the framework outlined above.
2 Trypanocides and their alternatives

Trypanosomosis is arguably the most important livestock disease in Africa. Animal reservoirs are also important in the epidemiology of Human African Trypanosomosis or sleeping sickness. (A significant disease of poverty, sleeping sickness ranks number 11 in terms of annual deaths from infectious diseases\(^1\).) There are three main strategies for managing animal trypanosomosis: vector control/eradication, use of trypanotolerant breeds and the use of trypanocides.

- **Vector control** is technically effective, but expensive and has only been possible where external support is available. Typically funded by donors and executed by governments or projects, large-scale control programmes have cleared less than 2% of the tsetse habitat\(^2\). Vector-control techniques include release of sterile insects, insecticide spraying, habitat change and removal of wildlife hosts; currently, the most used approach is bait technology (animals or fabrics that attract and kill flies\(^3\)). In recent years, interest has grown in community-managed and funded vector control; though also technically effective, sustainability has been very low, uptake outside projects negligible and auto-financing elusive\(^4\). However, when drug resistance is high, vector control is one of the few feasible options for trypanosomosis control and with increasing resistance, vector control may be increasingly adopted. Most current vector-control methods involve insecticides to kill tsetse flies. Although resistance to insecticides is also documented, it is thought unlikely to be a problem in tsetse control as the low population density and slow reproduction of tsetse flies do not favour rapid genetic change. However, inappropriate use of insecticides may lead to disruption of enzootic stability and consequent upsurge in tick borne diseases, resistance to insecticides in ticks, risks to human health and adverse environmental effects\(^5\); rational use principles should apply to insecticide use just as much as to medicine use.

- The use of **trypanotolerant** taurine cattle has been promoted, and farm trials show that they can be productive in terms of meat and milk\(^6,7\). However, in the mixed farming systems that predominate in much of sub-Saharan Africa, traction is the main priority, and farmers consider trypanotolerant cattle less suitable as draft animals (being smaller, slower and less tractable) and less profitable as investments (reflected in their lower sale price\(^8\). More than three-quarters of the cattle in tsetse-affected areas are non-taurine, and taurines are likely to remain a minority choice for the foreseeable future. Trypanotolerance is not an absolute phenomenon and in areas with high infection challenge or where cattle are stressed (by poor nutrition, plowing or other disease), trypanocidal drugs are required for animals to be productive\(^9\).

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Uptake</th>
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<tbody>
<tr>
<td>Vector control</td>
<td>2% of tsetse infested area is currently being controlled</td>
</tr>
<tr>
<td>Trypanotolerant animals</td>
<td>20% of cattle at risk are trypanotolerant</td>
</tr>
<tr>
<td>Trypanocides</td>
<td>70% of cattle at risk are treated</td>
</tr>
</tbody>
</table>

*Note: References are given in the text.*

- Although vector control and genetic resistance have potential for greater uptake, using **trypanocides** remains the single most important deliberate strategy for managing trypanosomosis. Used in all cattle-keeping communities at significant risk of trypanosomosis, this is the only control strategy which has proven sustainable and sufficiently attractive to be adopted spontaneously. However, trypanocide usage by farmers has received little attention or support from donors (in contrast to the heavily financed, but universally unsustainable, unattractive or unachieved options of vector control, trypanotolerance and vaccines\(^10\)). The management of trypanosomosis to a large extent depends on correctly using trypanocides and safe-guarding their efficacy by the prevention and containment of resistance. These objectives can be achieved through the promotion of rational and judicious drug use (which encompasses using alternatives to drugs and the rational use of insecticides).
Box 1: Trypanocides used in Africa

Five trypanocides are currently used in Africa: diminazene aceturate (DIM) has a short duration of action and is mainly used for treatment; isometamidium chloride (ISMM) is used for prophylaxis, metaphylaxis and cure; homidium salts are similar to ISMM but have a shorter period of protection (and are not widely available in West Africa); quinpyramine is licensed only for camels (because of its ability to induce cross-resistance to isometamidium and diminazene); and finally melarsomine which is recommended for camels and under development for use in other species. With the exception of melarsomine, current trypanocides have been in use for more than 40 years. Given the high price of de novo product development (estimated at more than US$ 800 million11) and the small African market for trypanocides (estimated at US$ 20 million per annum12), no new drugs are likely to emerge in the near future.
3 Rational use, irrational use and resistance

Modern medicines have made dramatic differences to human and animal health; at the start of the third millennium, the world population of both is without precedent (six billion humans and 20 billion domestic animals\(^\text{[13]}\)). In developing countries, veterinary drugs are widely used in even the most remote communities\(^\text{[14]}\), a trend that has accelerated since the liberalisation of economies in the 1980s. Used properly, veterinary drugs prevent loss, permit higher levels of production, improve animal welfare and safeguard the livelihood assets on which 700 million poor farmers in developing countries rely\(^\text{[15]}\). Used improperly, veterinary drugs waste scarce resources, occasion avoidable sickness and death, mask poor production methods and unnecessarily promote drug resistance.

While the costs of inappropriate treatment and lost production are met largely by the farmer who misuses the product, the costs of drug resistance are met by society and future generations. These include direct costs from additional treatments, persistent illness and higher mortality, as well as indirect costs from lost agricultural development opportunities. The costs of trypanocide resistance are unknown, but resistance costs can be high (for example, in human health, it is estimated that anti-microbial resistance costs up to US$ 350 billion \textit{per annum}\(^\text{[16]}\)). Resistance has developed to all anti-microbials used in non-trivial amounts, and is a function of both quantity and quality of use, with \textit{over-usage} and \textit{under-dosage} seen as key eliciting factors. There is abundant evidence that human pharmaceuticals are unnecessarily and improperly used in developing countries\(^\text{[17-21]}\), and that this has contributed to high levels of resistance\(^\text{[22]}\). The reasons for this irrational drug use in human medicine have been well described (Box 2)\(^\text{[23]}\) and many of these are likely to apply to the irrational use of veterinary medicines including trypanocides.

\begin{table}[h]
\caption{Box 2: Factors contributing to irrational drug use}
\begin{itemize}
\item Information gaps among policy makers, service providers and product/service users
\item Economic incentives such that product sellers and service providers gain money from over-treating
\item Medication culture which has strong social and cultural norms of treatment seeking (‘a pill for every ill’)
\item Promotional pressure and over-zealous marketing by pharmaceutical companies
\item Defensive medicine, with health-care providers over-treating through fear of adverse effects
\item Polypharmacy or multiple treatments resulting from diagnostic uncertainty (‘shot-gun therapy’)
\item Attribution errors so drug effectiveness is overestimated because of ignorance of natural course of diseases, reciprocity norms and cognitive biases
\item Information and supply gaps, with the result that alternatives to drugs are underused
\item Imperfect markets cause low availability of drugs and distorted prices
\item Poverty of product-users, such that they cannot afford full courses and appropriate doses of drugs.
\end{itemize}
\end{table}

Worldwide it is estimated that over half of all medicines are prescribed, dispensed or sold inappropriately and half of all patients fail to take their medicines correctly\(^\text{[24]}\). In response to widespread concerns over the use of human medicines, the World Health Organization (WHO) has been promoting the concept of \textbf{Rational Drug Use (RDU)} since the 1980s. RDU occurs when medicines appropriate for the disease are administered correctly for adequate time periods and at the lowest cost to the client and their community\(^\text{[1]}\). As such, the concept of RDU explicitly incorporates the externality of drug resistance (albeit partially). Analogous concepts of \textbf{appropriate drug use} and \textbf{judicious drug use} place more emphasis on safe-guarding treatment efficacy through minimising resistance. For example, judicious use is defined by the American Food and Drug Administration
(FDA) as ‘Use that maximizes therapeutic effect while minimizing the development of resistance’, and WHO’s Global Strategy on Microbial Resistance defines the appropriate use of antimicrobials as ‘the cost-effective use of antimicrobials which maximizes clinical therapeutic effect while minimizing both drug-related toxicity and the development of antimicrobial resistance’. In veterinary medicine, the concepts of prudent drug use and responsible drug use are also used (with the imprimatur of the Organisation Internationale des Epizooties, the veterinary equivalent of the WHO). These definitions also take into account that inappropriate use of drugs in domestic animals can cause zoonotic infections, food-borne diseases and residues or resistance problems for people.
Rational Drug Use principles applied to trypanosomosis

In contrast to the extensive literature on inappropriate usage of human pharmaceuticals by both public and professionals, there is little information on how farmers and animal health professionals use trypanocides and their alternatives. Usage affects resistance in two ways. Firstly, the quantity of use, and secondly, the quality of use (where quality includes drug choice, content, reconstitution, posology, administration and storage). A rough estimation of quantity of use can be obtained by dividing the market for trypanocides (estimated at 20-35 million US$) by the cattle at risk (estimated at 40-60 million); as one dose of trypanocides costs around 0.25-1 US$, this corresponds to about 0.5 to 2 treatments per cattle head per year. Given that trypanosomosis is usually hyper-endemic, most cattle will have at least one illness episode a year, so the quantity of drug use is not excessive from a clinical perspective. In Burkina Faso, there are 2.7 million cattle in tsetse-infested areas and 7 million doses of trypanocides used per year, corresponding to just over 2 treatments per animal per year, again not an excessive level. Indeed some studies indicate that many animals are untreated; in the 80s, Ilemobade estimated that trypanocide use overall was only one tenth of that indicated and a more recent study in Zambia found that only 50% of trypanosome infections were treated, almost all of these by farmers.

It is likely that the majority of trypanocide treatments are given by farmers or informal sector providers, because the majority of all animal health treatments in sub-Saharan Africa are given by farmers or the informal sector, and there are insufficient professional providers to individually treat the numbers of animals receiving trypanocides. In the project area of rural Kenedougou, for example, there are 70 thousand animals and one veterinary professional legally providing clinical services. It is prima facie obvious that one person will not be able to personally diagnose and treat more than a small number of the many thousands of animals at risk for trypanosomosis. Studies in East and Central Africa have shown a majority of farmers use modern veterinary products, and significant amounts of these are provided by the informal private sector. (The situation is analogous to that of human medicine where up to 80% of treatments in developing countries are self-medication, and prescription-only drugs such as antibiotics are widely available without prescription.)

As regards quality of use, it is often assumed that usage patterns are irrational because of widespread resistance, anecdotal reports of poor practice, the fact that most treatments are by non-professionals and analogies from human medicine. In fact very little is known about actual usage. The study in Zambia cited above indicated that farmers were using correct drugs at higher than recommended dosages and most did not reconstitute the drug correctly, but did not address the quality of administration or product. A study in Kenya found that nearly half the trypanocide treatments were given for diseases other than trypanosomosis. This may not be irrational, as where prevalence is high, trypanosomosis often underlies other disease, and if so trypanocides can be beneficial. Another Kenyan study found that side-affects were unusual when drugs were given by professionals and common when administered by farmers. Farmers routinely used extra-label intravenous injection because they had found that intramuscular injections led to high levels of abscesses, an indication of poor administration quality. The current project finds mixed evidence on rationality and appropriateness of treatments by farmers (section 6.3).

Indeed, it is possible that poor quality use by farmers is over-estimated. Resistance seems less common in villages than in situations where drugs are used intensively under professional supervision and following manufacturer’s guidelines, such as on ranches and in development projects. In these cases, resistance is often extreme and trypanocides are unsuccessful in controlling disease even when given at high dosage and short intervals, resulting in high mortality and morbidity. In cases where high levels of resistance are found in village systems, this may be because of cross-resistance rather than poor quality of use. There are some characteristics of
trypanocide use which should allow farmers to develop more competence than is the case for self-
medicating human patients (Table 2).

**Table 2. Why farmers may be more rational than patients.**

<table>
<thead>
<tr>
<th>Trypanocide Use by farmers</th>
<th>Self-medication by patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trypanosomosis has a high prevalence and most farmers have many animals, and so more opportunities to develop skills</td>
<td>Fewer disease episodes, so less opportunity to develop diagnostic skills</td>
</tr>
<tr>
<td>Cost-benefit considerations important, so less incentive to continue with ineffective treatments</td>
<td>Powerful cultural imperative to treat even when treatments are ineffective or very expensive</td>
</tr>
<tr>
<td>Few professional service providers so farmers have greater need to develop skills</td>
<td>More professional service providers available</td>
</tr>
<tr>
<td>Few drugs available, but these used for many years, giving more opportunity to attain familiarity and competency in use</td>
<td>Many different drugs, and new drugs continuously marketed</td>
</tr>
</tbody>
</table>

Literature is also lacking on the quality of drug use by veterinary professionals; irrational use by human health providers has been often documented in developing countries. (Surprisingly, there is little evidence that differences in prescribing patterns are related to different levels of training in human medicine. Similarly, the above mentioned Kenyan studies found little difference between animal-health service providers with differing levels of training and education.) Anecdotal evidence suggests that, like their counterparts in human medicine, veterinary professionals in developing countries often lack basic equipment, spend little time with patients and rarely perform clinical examinations, factors that will predictably result in inappropriate drug use.

The quality of veterinary products has received considerably more attention than the quality of use. Major concerns include counterfeit, smuggled and improperly kept drugs. A small number of studies have been carried out on trypanocide quality; all have found that substantial numbers of drugs contain insufficient amounts of the active ingredients. Some studies indicate that levels of sub-standard drugs were higher in products bought in the informal sector, others find no difference. Unfortunately, it is very difficult to estimate the real level of fake or sub-standard trypanocides as the few surveys reported either do not give details on the sampling methodology used or use methods which do not allow reliable extrapolation of their findings.
5 Promoting Rational Drug Use

Although proper drug use is key to managing both trypanosomosis and resistance, there is surprisingly little information on specific initiatives to improve veterinary drug use in developing countries. (However, using drugs appropriately is often a component of community animal-health programmes, for which there is an abundant literature). In human medicine, interventions to promote rational use have been widely implemented and offer insights on how to promote the rational use of trypanocides.

Most interventions have focused on the public health sector, some on use by private doctors, few on private pharmacies and very few on the informal sector (despite the fact that the majority of human health care takes place in the informal sector). Well-designed interventions can result in considerable impact. Ross-Dengen reviewed 59 studies on improving drug use which mainly took place in developing countries. Of the studies which were analysable, more than 40% resulted in high impact (>25% improvement over controls) and almost 40% had moderate impact (10–25% improvement over controls). Cost-benefit analysis is rarely carried out, but the few studies that have done this generally show marked benefits.

Evidence-based health care

Several important recent reviews have specifically addressed how rational drug use can prevent and contain antimicrobial resistance. The most credible of these use an evidence-based approach to assess the causes of resistance and the effectiveness of interventions to contain and prevent resistance. Evidence-based healthcare is emerging as the lead field in health care policy. It is defined as the conscientious use of current best evidence in making decisions about the delivery of health services, where current best evidence comprises up-to-date information from relevant, valid research about the efficacy, safety and efficiency of different forms of health care, the accuracy of diagnostic tests, and the predictive power of prognostic factors. Evidence is ranked hierarchically according to its quality using standardised criteria (an example of one such framework is given in Table 3) and higher levels of evidence are preferred over lower levels of evidence in making decisions.

Table 3. Hierarchy for assessing quality of evidence on effectiveness of rational drug use interventions.

<table>
<thead>
<tr>
<th>Rank</th>
<th>Method used for evaluating effectiveness</th>
<th>Category</th>
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<tbody>
<tr>
<td>1</td>
<td>Systematic review of all randomised control trials, including assessment of methodologies</td>
<td>Experimental (meta-analysis/review)</td>
</tr>
<tr>
<td>2a</td>
<td>One or more well-designed randomised control trial</td>
<td>Experimental</td>
</tr>
<tr>
<td>3a</td>
<td>Well designed before and after studies with control, or time series (with or without control)</td>
<td>Quasi experimental</td>
</tr>
<tr>
<td>3b</td>
<td>Well-designed cohort or case control studies (studies with concurrent controls are better than those with comparable controls)</td>
<td>Quasi experimental</td>
</tr>
<tr>
<td>3c</td>
<td>Well-designed case control studies</td>
<td>Non experimental</td>
</tr>
<tr>
<td>4a</td>
<td>Dramatic effects from uncontrolled experiments</td>
<td>Quasi experimental</td>
</tr>
<tr>
<td>4b</td>
<td>Descriptive studies, ex ante and post hoc evaluation of interventions</td>
<td>Non experimental</td>
</tr>
<tr>
<td>5</td>
<td>Expert opinion, theoretical derivations, analogies</td>
<td>Non experimental</td>
</tr>
<tr>
<td>6</td>
<td>General opinion</td>
<td>Non experimental</td>
</tr>
</tbody>
</table>

The concept of evidence-based healthcare complements that of rational drug use by providing an objective methodology for assessing the most rational quality and quantity of drugs, and the most effective interventions for attaining this. This is especially important in developing countries where many of the policy issues concerning animal health drugs and services are contentious, prone to
capture by powerful and entrenched interest groups, and debated with little involvement of important stakeholder groups. In this policy arena, credible and accepted frameworks to assess competing claims, entitlements and demands are desirable, and the combination of evidence-based health care and rational drug use represents the current best practice decision-making.

Evidence-based interventions that improve drug use

This report adopts an evidence-based approach to identifying and developing interventions to promote rational use of trypanocides. In the absence of trypanocide-specific literature, the conclusions of evidence-based meta-reviews and meta-analyses on interventions to promote rational drug use in human medicine are used as the best available guidance (see end notes 57–62). Interventions are usually categorised as: informational/educational; managerial; regulatory; and economic incentives. In practice, a combination of interventions is often used and synergies and trade-offs should be taken into account.

Informational/educational interventions

Informational/educational interventions involve providing information or training to health providers or users. They are politically unthreatening and easy to implement, and have been the most widely used intervention. Methods used include mass media, provision of printed material, continued professional development, counselling, training of groups or individuals, and academic detailing. The multiple reviews and evaluations agree that:

Success is greater (often >20% improvement) when:
• Multiple channels of information provision are used and multiple sessions take place
• A problem-oriented approach is followed
• There is focus on a single issue
• Participatory and interactive approaches (including peer review) are used
• Methods which target users as well as providers are used
• Training occurs in the work-place
• Local opinion leaders and role models are involved.

Strategies which have been successful in developed countries include:
• Academic detailing (educational outreach) where trainers visit individual professionals
• Decision-support systems (mainly computer-based) to change prescription behaviour.

Strategies which have little impact include:
• Mass media approaches – changes in behaviour are commonly 10% or less\(^66\). (But in large populations, even small changes in behaviour may be worthwhile and cost-effective)
• Dissemination of printed information and guidelines are consistently unsuccessful in improving prescriber behaviour\(^67\)
• Passive educational methods have little effect on behaviour change\(^68\).

Managerial initiatives

Managerial interventions shift the way services are delivered into more preferred paths and are potentially powerful ways of encouraging rational drug use. Using informational interventions, it is easy to create awareness but imparting knowledge and skills is progressively more difficult and changing behaviour more difficult still; improvements are often small and behaviour change prone to back-sliding. Managerial interventions change behaviour by restricting opportunities to deviate from norms; they provide guidance in the decision-making process, often backed by monitoring, rewards and sanctions. An important caveat is that there should be effective management in place, often not the case for public services in developing countries\(^69\). However, managerial initiatives may be effective in the private sector, providing businesses have incentives to comply with initiatives, and initiatives do not counter their economic interests. Managerial interventions have
even been successful when used in the informal (illegal) private sector\textsuperscript{70}. Effective managerial interventions include:

- Lists of essential drugs and formularies
- Evidence-based standard treatment guidelines (non-statutory standards)
- Drugs/therapeutics/ethics committees
- Peer review and learning structures
- Audit and feedback of prescribing practice
- Performance targets
- Price and quality information (score cards, ranking, quality marks)
- Course of therapy packaging
- Dispensing and prescribing controls.

Regulatory initiatives

Regulatory initiatives are widely promoted (with the failure of regulation usually seen as justifying more regulation). Among the most common regulatory initiatives in human and veterinary pharmacy are:

- Restriction of antimicrobials to prescription only
- Licensing manufacture, importation, distribution and sale of drugs
- Registration and inspection of drug sellers
- Standards-based marketing authorisation and registration of drugs
- Quality control of products and services
- Professional bodies to regulate conduct and quality of health service providers and education
- Restrictions on sales promotion and advertising.

Effective regulation can have significant impacts on rational use and reduction of resistance. For example, Spain (with poorly implemented legislation and antibiotics freely available from pharmacies) has higher antibiotic resistance than comparable European Union countries where regulation is implemented.

The problem with regulation is that most drug rules are against the economic interests of those regulated, and have proven very difficult to implement and sustain. Less than one in six WHO country members have well-developed and implemented drug regulation; unsurprisingly these are mainly industrialised and rich countries\textsuperscript{71}. Very few developing countries have operational licensing, inspection or quality control systems for human drugs\textsuperscript{72}. The problem is often implementation failure rather than absent or inadequate policy and regulations. Implementation failure has multiple causes, none of which are likely to be resolved in the near term: poor governance, financial constraints, inadequate human resources, lack of information, weakness of consumer and professional groups and low prioritisation of pharmaceutical regulation are often cited\textsuperscript{73}. Moreover, human and animal drugs are exceedingly difficult to control in a liberalised market (due to high consumer demand, low substitutability, high value-to-volume ratios, and being quality-assured by brand rather than source). Experience from other fields suggests that attempting to regulate the supply of such products risks forcing the trade underground with often worse effects\textsuperscript{74}. As long as universally effective regulation of human medicine remains a desired but largely unobtainable ideal, it may be naïve to consider effective regulation of veterinary products as an attainable near-term goal.

The regulatory conceptualisation of the pharmaceutical sector is that of ‘command and control regulations’, i.e. centrally-promulgated diktats that restrict activities using credible threats of sanctions. There has been some interest in more flexible and participatory approaches to regulation, for example, tripartite regulation, decentred regulation, and self/peer regulation\textsuperscript{75,76}. Another recent development is a focus on assessing the costs and benefits of regulation (regulatory impact
However, these approaches have not as yet been applied to the pharmaceutical sector.

Economic incentives

Economic incentives or market-based instruments change behaviour by providing financial reward or imposing financial costs. Although often considered as an alternative to regulation, they require some legislation and regulation for their creation and function. Theoretically more effective and less costly than command and control regulation, they have been little used in the pharmaceutical sector in developing countries. Economic incentives currently used or suggested include:

- Subsidies/taxes on pharmaceutical products to influence price and hence purchasing behaviour
- Competition in the provision of health services and products to decrease price and drive up quality
- Pharmacy cross-subsidies to encourage service provision in under-served areas
- Tax breaks for compliance with regulations, research, or relocation to rural areas
- Orphan drug provisions to incentivise new products for neglected diseases
- Increasing patent length, height and breadth to encourage manufacturers to internalise resistance costs, and develop drugs with new modes of action rather than ‘copy-cat’ products
- Removing/placing tariff and non-tariff barriers to pharmaceutical trade
- Stimulating research and development by surrogate markets or tournaments/prizes
- Tradable permits for resistance.

Price is the single most important determinant of quantity of drug use, although it appears to have little effect on the quality of drug use. When Iceland stopped subsidising antimicrobials, use and resistance fell, although both remained high in similar countries which continued to subsidise. (The greater effectiveness of price than information is illustrated by a case study in California; a major anti-smoking media campaign resulted in a reduction of 232 million packs. Increasing the tax on cigarettes led to a reduction of 1.3 billion packs.) However, instruments based on price control, subsidies, taxes and financial incentives will only work if there is financing and high levels of governance, which is often not achievable in developing countries. Furthermore pharmaceutical markets are complex and imperfect and market-based interventions may have non-obvious effects or perverse effects. The Commission on Macroeconomics and Health found that reducing tariffs on pharmaceuticals was paradoxically more likely to increase final pharmaceutical prices than to reduce them (by undermining low-cost domestic producers).

Even when economic incentives exist, they may not produce desired results. For example, orphan drug provisions in the USA (and to a lesser extent in the EU) incentivise the development of new products for neglected tropical diseases through research grants, tax breaks and lower registration costs. Eflornithine, the first new drug against human trypanosomosis for more than 40 years, received orphan drug status from the American Food and Drug Administration in 1990. However, within a few years production was discontinued because of low sales. The license was offered to the WHO, but it was not possible to find a manufacturer who could produce the drug at costs affordable to users. Eflornithine went out of production, and by 2001 less than 1000 doses remained. Fortunately, the discovery that eflornithine could be used as a facial hair remover (for which there is large market in developed countries) allowed its continuing production, but the case illustrates how markets work on bottom-line principles and that even with interventions, may not guarantee essential drugs for those with great need but little purchasing power.

Other macro policy interventions to contain and prevent microbial resistance (such as legislation change, global control of drug availability, patent laws, and competition policy) are considered to have potential to contain and prevent resistance, but there is relatively little information on their

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1 Orphan drug incentives are intended to encourage research, development, and marketing of products for diseases and conditions that would otherwise be under funded. These are common in developed countries, for example, Japan, USA, EU, Singapore and Australia all have well developed programmes.
application and impact. A promising recent trend are initiatives by development agencies to create surrogate markets through purchase commitments or tax-breaks for the drugs that treat neglected diseases (seriously disabling or life-threatening diseases for which treatment options are inadequate or do not exist, and for which the drug-market potential is insufficient to attract a private-sector response\textsuperscript{82,83,84}.) Human trypanosomosis is considered a candidate for these\textsuperscript{83,84} with possible spill-over benefits to animal trypanosomosis if new treatments can be found.

A major constraint to the more widespread use of policy and economic interventions in the management of trypanocide resistance is the lack of compelling evidence on the costs of resistance or its impacts on farmers and national economies, and the absence of powerful lobbying and advocacy groups able to represent those most affected by the problem.
A framework for promoting Rational Trypanocide Use

Promoting RDU (and by doing so enhancing trypanocide resistance management) requires a problem-oriented and purposive approach. The WHO recommends clearly defining the problem (formative studies) followed by developing interventions using criteria of impact (magnitude, probability and unintended impacts), feasibility (technical, political, cultural and economic) and assessing availability of donor support. Promising strategies are then trialled with intervention and control groups (intervention studies). Occasionally, unambiguous evidence of effectiveness may warrant national programmes and policy change; more commonly revision and restudy is indicated or the intervention proves to be ineffective.

Following these principles, a framework can be developed for promoting Rational Trypanocide Use within the context of Kenedougou. The framework used was explicitly evidence-based, but because of many gaps in information, evidence was at the lower levels of the hierarchy. The framework consists of the following five steps:

1. Assessment of the prevalence and impact of trypanosomosis, and extent and impact of resistance
2. Understanding the policy and practice of trypanocide use at national and best-practice level
3. Understanding the fail-points of Rational Trypanocide Use
4. Identification of options to address fail points
5. Implementation and evaluation of best-bet interventions

The rest of the section shows how this framework was applied to the Kenedougou project, highlighting the lessons learned and wider implications.

6.1. Assessing the prevalence and impact of trypanosomosis and the impact of resistance

The prevalence of trypanosomosis has been well characterised in Kenedougou, Burkina Faso, much of this work being carried out by the first phase of the current project. A cross-sectional study in 1998 covering 45 of the 166 villages of Kenedougou showed a high parasitological prevalence of trypanosomosis in the two southern districts (10.5% and 10.0%), lower prevalence in the central district (4.2%) and low prevalence in the north (1.4%). This was followed by an ISMM block treatment trial in nine villages with high prevalence in order to characterise drug resistance. It found a fail-rate of 37.7% after ISMM treatment and 18.0% after DIM treatment. Resistance was confirmed using laboratory tests. A socio-economic study in six villages showed that farmers used considerable amounts of trypanocides, but the study did not find significant differences in cattle ownership, area cultivated or trypanocides purchased between villages with different levels of drug resistance. A longitudinal study carried out in four villages to assess productivity impacts found that calves that were more frequently positive for trypanosomosis tended to weigh less.

Although parasitological, entomological and haematological impacts have been well-described, there is less information on the direct impacts of trypanosomosis and resistance on animal health and productivity and the impact of this on farmers’ livelihoods. However, from research carried out in other areas, some estimates can be cautiously applied to Kenedougou (Table 4). These estimations represent an endemic situation with some control activities by farmers; and do not take drug resistance into account.
Table 4. Likely benefits of trypanosomosis control applied to livestock in Kenedougou.*

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Magnitude</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased calf mortality</td>
<td>Doubled</td>
</tr>
<tr>
<td>Decreased cow mortality</td>
<td>Halved</td>
</tr>
<tr>
<td>Decreased age at first calf</td>
<td>3 months</td>
</tr>
<tr>
<td>Decreased calving interval</td>
<td>1 month</td>
</tr>
<tr>
<td>Decreased abortions and still births</td>
<td>From 2 to 10%</td>
</tr>
<tr>
<td>Increased reproduction rate</td>
<td>By 10% (across a range 40 – 60%)</td>
</tr>
<tr>
<td>Increased traction</td>
<td>1 more hectare (for farms of 1–7 hectares)</td>
</tr>
<tr>
<td>Increased milk</td>
<td>Around 25 kg per lactation</td>
</tr>
<tr>
<td>Increased weight at weaning</td>
<td>Around 10 kg per calf</td>
</tr>
<tr>
<td>Increased cow weight</td>
<td>Around 10 kg</td>
</tr>
<tr>
<td>Decreased trypanocides purchase</td>
<td>By 60%</td>
</tr>
</tbody>
</table>

In the current project, Participatory Rural Appraisals and household Knowledge Attitude Practice (KAP) questionnaires show that farmers consider trypanosomosis to be the most important disease of livestock. For agro-pastoralist farmers, the most important negative impacts are decreased traction and costs associated with drugs, while for pastoralists, the most important impacts are mortality and decreased milk production.

There have been no studies on the impact of drug resistance per se but it can be assumed that the additional costs of drug resistance are related to losses due to increased morbidity and mortality of trypanosomosis in the cases where treatment fails, plus costs of additional treatments given as the result of treatment failure. However, there are some caveats when assessing the impacts of resistance:

- Drug resistance generally follows a sigmoid curve, with a final equilibrium point usually less than 100% (depending on the selection pressure and the change in fitness associated with resistance) and this is probably true for trypanocide resistance. The costs of resistance (and hence the benefits of containing resistance) in any given situation will depend on the location on the curve.
- Even when resistance is very high, trypanocides can have beneficial effects; they do not eliminate resistant infections, but may improve the animal’s ability to cope with them. Acceptable levels of production have been attained (at least in the short term) in the presence of high resistance, through the use of trypanocides.
- Drug resistance is a gradual phenomenon allowing opportunity for animals and farming systems to adapt. It is unlikely to result in the catastrophic losses seen when naïve animals are exposed to trypanosomosis for the first time.

Assessing the prevalence and impact gives information on the level and significance of the problem and hence a guide to the resources that might be reasonably devoted to attempting to resolve the problem. It is clear that trypanosomosis and drug resistance is a significant constraint to farmers in southern Kenedougou and one that is likely to have considerable adverse impacts. More information on the direct and indirect impacts is needed; if control is to be paid for by farmers, their perceptions of cost and benefit must also be taken into account.

6.2a. Understanding the policy and practice of animal health product use: National policy

The policy of veterinary medicine in Burkina Faso restricts the administration of trypanocides to veterinarians. The sale of trypanocides to the public is theoretically by a) pharmacists who sell trypanocides only under prescription of a veterinarian, b) registered private veterinarians using trypanocides on animals under their care, and c) a small proportion of public veterinarians who are mandated to provide clinical services (most public sector veterinarians are supposed only to
provide extension and regulation functions). Wholesalers can only sell to retailers, and not directly to the public. Only a few trypanocides have been licensed for use in Burkina.

In practice, trypanocides are widely used by livestock keepers and often purchased in the informal sector or in veterinary pharmacies in neighbouring Mali. In a typical village, 100% of farmers use trypanocides and antibiotics, more than 80% of treatments are by the farmers themselves, and more than 80% of drug sales are by non-professionals. The market share of the informal-sector is also indicated by the high number of informal-sector service providers. For example, in Orodara, the provincial capital for Kenedougou, there are no private-sector pharmacies or veterinarians, one veterinary agent with a very limited supply of veterinary products, and 20 informal-sector drug sellers. Similarly, the range of trypanocide brands is greater in practice than policy. Many trypanocide brands are licensed (or are unlicensed but available) in Mali and prices are lower than in Burkina Faso. The rapid appraisal of the informal sellers in Orodara market showed that most of the 20 vendors sold trypanocides originating from Mali.

Kenedougou lies in the sub-humid zone and veterinary services and development projects have recommended that all the cattle in the herd are given regular treatments with ISMM by a veterinarian at the beginning and the end of the rains to prevent trypanosomosis (prophylactic use), and that sick animals are treated by a veterinarian with DIM (curative use). In practice, this policy is almost impossible to follow for economic and logistical reasons, and has the adverse effect of encouraging farmers to conceal animal health care behaviour. Farmers typically report that veterinary agents treat 100% of sick animals and 100% of animals receive ISMM, but this is contradicted by more detailed studies and triangulation.

Understanding the policy framework helps ensure that interventions are legitimate and coherent with government aims. Because it is not legal for farmers to treat their animals with trypanocides, the project adopted a drug consumer rather than drug user approach. Farmers were not trained to give injections but to understand what a good injection is. Understanding current practice ensures that information provided is useful and meets the needs of recipients. Previous projects had assumed that farmers know very little and treatments are always given by veterinarians, and hence provided information that was too basic for farmers’ needs.

6.2b. Policy and practice of trypanocide use — best practice guidelines

Expert opinion agrees that resistance to trypanocides can best be avoided and contained by reducing the selection pressure (i.e. decreasing the quantity of use), and avoiding treatment regimes that expose trypanosomes to sub-inhibitory drug concentrations, mutagenic drugs, or drugs that induce cross-resistance (improving the quality of use). Specific recommendations include:

- Decrease the quantity of trypanocides used
  a. Promote alternatives (vector control/avoidance and trypanotolerant animals)
  b. Avoid mass treatments at short intervals
  c. Avoid unnecessary treatments.
- Avoid exposing trypanosomes to trypanocides at low doses over long times
  a. Don’t under-dose
  b. Avoid mass prophylactic treatments at irregular intervals
  c. Treat only clinical cases.
- Use sanative pairs
- Avoid drugs that induce cross-resistance (for example, quinpyramine in cattle).

Some frameworks give more detailed guidance on action appropriate for different levels of resistance, an approach that allows tailoring to the specific situation (Table 5). A constraint to this

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1 This might be ethically objected to – it is a priori likely that farmers will use the information to improve the way they give injections. However, in the context of a research project, and considering that working with informal providers has been carried out in human medicine, and after discussion with regulatory stakeholders, it was decided to use this approach.
approach is that data on levels of resistance are lacking, and very expensive to collect. In addition, general guidelines exist for management of trypanosomosis and computer-based decision support tools have been developed.

**Table 5. Guidelines for drug resistance.**

<table>
<thead>
<tr>
<th>Resistance to a single trypanocide</th>
<th>Multiple resistance</th>
<th>Use of ISMM</th>
</tr>
</thead>
<tbody>
<tr>
<td>0% prevalence</td>
<td>Sanative pairs</td>
<td>Avoid the use of continuous ISMM prophylaxis</td>
</tr>
<tr>
<td></td>
<td>Vector control</td>
<td>Consider the use of prophylaxis only in cattle exposed to heavy challenge for a defined period, e.g. transhumance or high seasonal challenge</td>
</tr>
<tr>
<td></td>
<td>Avoid high risk areas</td>
<td>Increase the proportion of trypanotolerant cattle</td>
</tr>
<tr>
<td></td>
<td>Avoid block treatments</td>
<td>Never administer ISMM more frequently than every 3 months</td>
</tr>
<tr>
<td>1 – 30%</td>
<td>Sanative pairs</td>
<td>Only treat clinical cases</td>
</tr>
<tr>
<td></td>
<td>Treat only clinical cases</td>
<td>Intensify vector control</td>
</tr>
<tr>
<td></td>
<td>Investigate trypanocide use</td>
<td>Consider zero-grazing or fly-proof stabling</td>
</tr>
<tr>
<td></td>
<td>Vector control</td>
<td>Increase the proportion of trypanotolerant cattle</td>
</tr>
<tr>
<td></td>
<td>Temporal and spatial surveillance</td>
<td></td>
</tr>
<tr>
<td>31 – 60%</td>
<td>Use sanative pair</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Monitor treatment outcomes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treat inter-current infections</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vector control</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Improve husbandry and nutrition</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Trypanotolerant animals</td>
<td></td>
</tr>
<tr>
<td>&gt;60%</td>
<td>Treat only clinical cases</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Zero-grazing</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vector control</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Trypanotolerant breeds</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Trypanotolerant species</td>
<td></td>
</tr>
</tbody>
</table>

In practice these guidelines are not well followed in Kenedougou:

- Guidelines and levels of resistance have not been communicated to drug manufacturers, service providers or regulatory authorities who still recommend practices that are contraindicated by the guidelines (for example, metaphylaxis and prophylaxis in the presence of resistance).

- Guidelines, levels of drug resistance and even the concept of drug resistance, have not been communicated to the farmers who carry out the majority of treatments, or to the informal sector which provides many treatments; communicating with these sectors is challenging as their activities lack legitimacy.

- Guidelines focus on what is technically desirable rather than what is socio-economically or institutionally feasible. The suggested alternatives to trypanocides (e.g. vector control, zero-grazing and trypanotolerant animals) may not be cost-effective or practical at present levels of development in Kenedougou.

- Lack of precision in some guidelines: for example, the concept of sanative pairs is used in at least four different ways, and some of these interpretations are not compatible with the guidelines.

- Lack of guidance on important practical questions, in particular:
  - whether (and if so, by how much) dosages should be increased in the presence of resistance
  - how refractory cases should be treated, given the pragmatic approaches used by farmers and veterinary agents of repeating doses, increasing doses, and changing brands
  - whether hygienic or sanative treatments are still recommended, given the presence of multiple drug resistance

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2 Use one of the pair until resistance appears, and then the 2nd until the resistant strains have disappeared (FAO); treat relapses with the other of the sanative pair (manufacturer’s recommendations, MR); Treat all animals with DIM 2 weeks before treating with ISMM / homidium to remove resistant infections (MR); Cattle maintained with ethidium prophylaxis or regularly treated with ethidium should receive an annual treatment with DIM to minimise resistance (MR).
- whether the innovation of treatment heterogeneity (randomly using the different drugs available rather than holding one drug in reserve) is applicable to trypanocides
- whether metaphylaxis (treating all animals in a herd when one becomes ill) is still a recommended strategy given its likely impact on resistance

- Lack of sensitive and specific pen-side tests makes the recommendation to treat only clinical cases difficult to comply with, especially as trypanosomosis is a cryptic disease and clinical signs are non-specific.
- Most treatments are given by farmers, but they lack information and skills to identify and treat inter-current infections and to monitor treatment outcomes.
- Surveillance is not used because of the high costs of estimating resistance, and the lack of prioritisation by national governments and donors.

In addition to these guidelines specific to trypanocide resistance, other widely recommended guidelines on containing and avoiding resistance to microbials include:

- Establishing surveillance and reporting systems
- Setting of threshold rates of resistance that trigger investigation and mitigation
- Carrying out risk analysis and cost-benefit analysis of drug use
- Providing stakeholders with information on drug use and drug resistance
- Including resistance prevalence data in product information (and updated every 5 years)
- Establishing an audit trail from drug producer to end-user
- Carrying out regulatory and policy impact assessments
- Following a regional approach to containment of resistance, with cross-boundary harmonisation
- Establishing expert authorities to provide advice
- Drafting, disseminating and adopting Evidence-based Use Guidelines as ‘the standard of care’
- Involvement of government and civil society in education
- Including drug resistance and RDU in the education of medical, pharmacy and veterinary professionals
- Recognising the importance of the private and informal sector and upgrading their skills
- Encouraging consumer organisations to take up the issue of resistance.

Best-practice guidelines need further elaboration and tailoring to the situation in Kenedougou, and should be communicated to all stakeholders.

6.3. Understanding fail-points in Rational Drug Use

The third step in the framework consists of understanding the fail-points in RDU. For Kenedougou project, a KAP household survey on trypanosomosis management was carried out in 10 villages (see Working Paper 8 in this series). This covered every cattle-owning household willing to participate (more than 80% of households). This survey was supplemented by Participatory Rural Appraisals using ethno-diagnostic tools. Epidemiological studies and village clinics provided further information on farmer diagnosis, and treatments. Although the data have not yet been quantitatively analysed, a qualitative assessment can be made of farmer drug use.

The following process (flow) chart of a therapeutic episode for trypanosomosis was constructed by farmers using participatory techniques. Although it simplifies the decision-making process by omitting alternative treatments, prophylactic treatments and supportive treatment, it allowed the identification of 10 potential fail-points for RDU.

Fail points in trypanocide (TC) use:
1. Ability to detect livestock illness
2. Presumptive diagnosis of trypanosomosis (differential diagnosis)
3. Decision to treat
4. Choice of treatment
5. Source of trypanocides
6. Quality of trypanocide
6.3.1. Ability to detect illness

Farmers appear to be good at recognising disease. During the epidemiological survey, farmers were able to identify the majority of animals subsequently found to be sick on the basis of parasitological tests and red blood cell counts. Farmers had few false negatives (animals sick on parasitological or haematological tests, which farmers thought were well), but some false positives (animals well by parasitological/haematological tests which farmers thought were ill). However, parasitological tests have poor sensitivity (possibly as low as 30% when compared to the gold standard of polymerase chain reaction tests) and some of the animals parasitologically negative may have been disease positive.

*Farmers detect the majority of sick animals.*

6.3.2. Presumptive diagnosis of trypanosomosis

Trypanosomosis is a cryptic disease, notoriously difficult to diagnose. The most common constellation of signs recognised by veterinarians (i.e. weight loss, anaemia, fever and lymphadenopathy)
are non-specific and inconstant, while the more specific signs (e.g. corneal opacity, paresis, and pica) are often absent or terminal. Farmer diagnosis of trypanosomosis was assessed through ethno-diagnostic focus groups work and a household KAP questionnaire. These showed that farmers intuitively use multiple tests for diagnosing trypanosomosis:

- Observation of behaviour (Table 6)
- Observation of physical condition (Table 6)
- Rule-out of other causes
- Assessment of risk factors.

Farmers rule out the other major causes of weight loss and weakness using the following criteria.

- Malnutrition: hungry, alert and seeks food
- Worms: eats but stays thin, diarrhoea and pot belly.

Farmers consider risk factors when making a presumptive diagnosis.

- Breed: zebu or crosses are more susceptible
- Season: end of dry season and rains are high risk
- Grazing: riverine galleries are high risk
- Watering: using village pumps is low risk.

The tests used by farmers are based on observation of appearance and behaviour, and farmers are not aware of tests based on clinical examination, e.g. taking of temperature, assessment of mucous membranes for anaemia, palpation of lymph nodes. Farmers’ general disease recognition skills are poor; they do not recognise many of the less common diseases that occur in Kenedougou. They do not practice differential diagnosis: when diagnosing, farmers look for evidence to confirm the diagnosis rather than to exclude it (an almost universal cognitive bias).

Accuracy of diagnosis depends on the prior probability of trypanosomosis and the specificity and sensitivity of the tests used to diagnose trypanosomosis. Under standard Bayesian decision-making theory, post-test probability is a function of pre-test probability and the strength of evidence (measured by the likelihood ratio). Because the pre-test probability of trypanosomosis is high (a reflection of the high prevalence, and effective rule-outs), farmer diagnosis is likely to be accurate. However, if the prevalence of infection falls (the result of vector control), then diagnostic accuracy will significantly deteriorate, unless more specific and significant tests are adopted. Studies suggest that irrationally high levels of treatment can persist after disease is reduced.

The majority of diagnoses are correct given the present prevalence of trypanosomosis. This is likely to change if the prevalence of disease changes. Differential diagnosis skills are poor.

6.3.3. Decision to treat

Farmers do not treat all animals that become ill with trypanosomosis, and chronically ill animals are present in all villages. There is little information on self-cure in the trypanosomosis literature, and although it is known that some cattle breeds can ‘tolerate’ infections without adverse effects, the standard recommendation is to treat clinically ill animals and parasitologically positive animals with low red blood cell counts. Farmers believe that many animals will self-cure in the rainy season, but very few animals will self-cure in the dry season.

Decision to treat depends on knowledge of treatment options, belief in the efficacy and necessity of treatment, availability of treatments and ability to pay for treatment. Initial survey work shows that farmers are aware of the treatment options (modern and traditional), believe that treatment is necessary and effective, and have good access to treatment. The most limiting factor appears to be price.

Many farmers treat sick animals themselves, especially farmers who own many animals. However, local experts (knowledgeable but untrained community members) also give treatments, as do ‘vaccinators’ (community members with basic training in animal health). A minority of farmers
seek treatment from veterinary professionals, often when treatment from other sources has been tried and failed.

**Farmers choose to treat many, but not all, sick animals. By conventional veterinary medicine standards, farmers are under-treating animals. However, the cost-effectiveness of under-treatment has not been evaluated and it is possible that under-treatment is an economically rational strategy. (It is also possible that under-treatment is causing avoidable losses from morbidity and mortality.) Under-treatment will not lead to drug resistance.**

**Table 6. Signs of trypanosomosis recognised by farmers.**

<table>
<thead>
<tr>
<th>Sign recognised by farmer</th>
<th>Validity, sensitivity, specificity</th>
<th>Indicator of</th>
<th>Test category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tears</td>
<td>Valid, fairly specific, non sensitive</td>
<td>Ocular involvement?</td>
<td>Observation</td>
</tr>
<tr>
<td>Corneal opacity</td>
<td>Valid, fairly specific, non sensitive</td>
<td>Ocular involvement</td>
<td>Observation</td>
</tr>
<tr>
<td>Licks the earth</td>
<td>Valid, fairly specific, non-sensitive</td>
<td>Nervous system involvement</td>
<td>Behavioural</td>
</tr>
<tr>
<td>Liquid under the chin</td>
<td>Valid, fairly specific, terminal sign</td>
<td>Oedema</td>
<td>Observation</td>
</tr>
<tr>
<td>Paralysis</td>
<td>Valid, non-specific, terminal sign</td>
<td>Nervous system involvement</td>
<td>Observation</td>
</tr>
<tr>
<td>No rumination in the morning</td>
<td>Valid, fairly specific</td>
<td>Fever</td>
<td>Observation</td>
</tr>
<tr>
<td>Ears held down</td>
<td>Valid non-specific</td>
<td>Fever</td>
<td>Observation</td>
</tr>
<tr>
<td>Nose is dry</td>
<td>Valid non-specific</td>
<td>Fever</td>
<td>Observation</td>
</tr>
<tr>
<td>No reaction when touched/bitten by flies</td>
<td>Valid non-specific</td>
<td>Malaise</td>
<td>Behavioural</td>
</tr>
<tr>
<td>Depression, especially in the morning</td>
<td>Valid non-specific</td>
<td>Malaise</td>
<td>Observation</td>
</tr>
<tr>
<td>Looks for a cool shady place</td>
<td>Valid non-specific</td>
<td>Fever</td>
<td>Behavioural</td>
</tr>
<tr>
<td>Skin sticks to the body</td>
<td>Valid non-specific</td>
<td>Dehydration</td>
<td>Examination</td>
</tr>
<tr>
<td>Bad odour from mouth</td>
<td>Valid non-specific</td>
<td>Ketosis</td>
<td>Observation</td>
</tr>
<tr>
<td>Separates from the herd</td>
<td>Valid non-specific</td>
<td>Malaise</td>
<td>Behavioural</td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>Valid non-specific</td>
<td>Malaise, fever</td>
<td>Behavioural</td>
</tr>
<tr>
<td>Dirty coat</td>
<td>Valid non-specific</td>
<td>Malaise</td>
<td>Observation</td>
</tr>
<tr>
<td>Staring coat</td>
<td>Valid non-specific</td>
<td>Malaise</td>
<td>Observation</td>
</tr>
<tr>
<td>Constipation</td>
<td>Valid non-specific</td>
<td>Digestive disturbance</td>
<td>Observation</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>Valid non-specific</td>
<td>Digestive disturbance</td>
<td>Observation</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Valid non-specific</td>
<td>Anorexia, fever</td>
<td>Observation</td>
</tr>
<tr>
<td>Nervous signs</td>
<td>Valid non-specific</td>
<td>Nervous system involvement</td>
<td>Observation</td>
</tr>
<tr>
<td>Breathes more rapidly</td>
<td>Valid non-specific</td>
<td>Anaemia</td>
<td>Observation</td>
</tr>
<tr>
<td>Chronic disease</td>
<td>Valid non-specific</td>
<td>Disease duration</td>
<td>Observation</td>
</tr>
<tr>
<td>Loses hair from the tail</td>
<td>Ethno-diagnostic literature only</td>
<td>?</td>
<td>Observation</td>
</tr>
<tr>
<td>Salivation</td>
<td>Not reported in literature</td>
<td>?</td>
<td>Observation</td>
</tr>
<tr>
<td>Refuses salt</td>
<td>Not reported in literature</td>
<td>?</td>
<td>Observation</td>
</tr>
<tr>
<td>Nasal discharge</td>
<td>Not reported in literature</td>
<td>?</td>
<td>Observation</td>
</tr>
<tr>
<td>Teeth grinding (bruxism)</td>
<td>Not reported in literature</td>
<td>?</td>
<td>Observation</td>
</tr>
<tr>
<td>Refuses to drink</td>
<td>Not reported in literature</td>
<td>?</td>
<td>Observation</td>
</tr>
</tbody>
</table>

6.3.4. Choice of treatment

Traditional treatments are commonly used. It is likely that these alleviate symptoms and possible that they have trypanocidal properties. Farmers recognise that traditional treatments may be
toxic if used incorrectly and consider them to be less effective than modern drugs. Traditional
treatments are often used as a first-line treatment; if they fail western drugs are used. Modern tryp-
anocides are known and used by nearly all farmers. They are considered to be effective, although
some farmers have noticed that they are less effective now than in the past (the result of drug
resistance?). DIM is preferred as a curative drug, although ISMM is used by a minority. Farmers
rarely give ISMM in the dry season as they believe it is ‘too strong’ for cattle weakened by mal-
nutrition. Many farmers use non-trypanocidal western drugs for trypanosomosis, mainly endo-
parasiticides, tetracycline capsules or injections and mineral/vitamin tablets. These are widely
offered on the informal market as ‘cures’ for trypanosomosis.

**Farmers usually choose the correct treatment for trypanosomosis. Market sellers often give
incorrect advice.**

6.3.5. Source of trypanocides

Farmers obtain drugs from a wide variety of sources, including other farmers, local experts, vaccin-
ators, cattle traders, informal market sellers, pharmacies, veterinary agents and private vets. It is
difficult to get accurate details drug sources, as farmers have received much didactic extension on
only using veterinarians to treat sick animals. Therefore, they tend not to reveal illegal sources.
Although sources vary between villages, it seems the most significant sources are other farmers,
vaccinators, the informal sector and pharmacies. Farmers say they use informal services because
they are cheap, convenient and the drugs work. Pharmacists have a wider range of products, better
advice and better conditions for storing medicines. Farmers are not well informed of distinctions
between service providers – veterinary agents and more sophisticated informal-sector providers
were often referred to as ‘private vets’.

**Farmers buy from sources that provide the products they need at prices they can afford,
generally pharmacists and the informal sector. However, the quality of advice is not good.**

6.3.6. Quality of trypanocides

The most knowledgeable farmers judge drug quality by external signs and physical characteristics.
They avoid packets that are faded, dirty and torn. They examine seals for evidence that packets
have been used and then refilled with fraudulent materials. By feeling the contents within the
packet they can detect if the seal is unbroken (the contents feels like sand), or if the seal has been
broken (the contents feel lumpy). They are aware of expiry dates. They know that products should
not be exposed to sun or excessive heat. They also are familiar with the colour and physical
characteristics of the re-constituted product. While able to detect ‘home-made’ forgeries, farmers
are less good at detecting professional forgeries, which often differ only slightly from the real
product. Fraudulent products do exist but there is no data on how widespread they are, however,
they do not seem to be present at a high level, as no examples have so far been found in the
course of the project despite ongoing efforts to locate them on the informal markets.

Little information is available on the pharmacological quality of trypanocides. Many studies have
been carried out on quality of human medicine and it is common for at least one fifth of the drugs
examined in developing countries to be defective\(^{101}\). One survey on trypanocides found that 24%
of preparations of diminazene contained less than 90% of the active ingredient\(^{102}\). Unfortunately
this study did not provide information on which brands were most likely to be defective, although
it may be reasonable to assume that small companies located in developing countries are less
likely to produce quality-assured drugs. (Interestingly there was no difference in quality between
drugs obtained from government services, private veterinarians, informal sector and pharmacies.
Similar results were found in a study on human drugs in Guinea\(^{103}\). However, other studies on

\(^{100}\)
veterinary drug quality have found high levels of sub-standard products, especially among drugs sold in the informal sector\textsuperscript{104}.

Farmers choose good products most of the time, but a significant number of products may contain less than 90\% of the active ingredient. This is not detectable by farmers (or for that matter, by professionals), and will result in under-dosage facilitating resistance.

6.3.7. Preparing injections and calculating dosages

Trypanocides are sold as powders to which water must be added in order to make an injection solution. Farmers do not know the correct quantity of water to add for dilution. They add a small amount of water usually less than the amount recommended. Farmers use clean, but not boiled, water to make up injections. Injections are made up in the packet or in small containers. If the latter are used, they are clean but have not been sterilised by boiling. Un-sterile injections lead to abscesses or sequestration, which is effectively an under-dosage as the product is not properly absorbed. Farmers do not calculate dosage by weight. They usually give one small sachet per animal; effectively an over-dosage\textsuperscript{40}. A minority of farmers reduce the dose if the animal does not seem very sick; however, most give a full dose. Vaccinators who treat many animals are more likely to under-dose than farmers treating one or two.

Farmers rarely prepare injections according to manufacturers’ recommendations, resulting in decreased efficacy which will facilitate resistance. Farmers do not calculate dosages according to weight; this may result in under or over-dosage, with only the former leading to resistance.

6.3.8. Administering injections

Administration technique is poor. Most farmers use the upper fore or hind limb, but these are not good sites, as there is a high risk of damaging nerves or vessels and if any infection is introduced the consequences are serious. Some farmers use the dorsal thorax; this is also unsatisfactory as there is insufficient muscle mass. Farmers do not know how to give deep intra-muscular injections, and many of their injections are superficial. Injection technique is also poor: Farmers do not split the dosage when large volumes are injected; they do not draw back on the syringe to check for blood; they do not place pressure on the site while withdrawing the needle to avoid spillage; they do not massage the injection site. These problems result in abscesses, sequestration, deposition of injection in sites from which it cannot be absorbed, and spillage of trypanocide. All of which reduce the amount of available trypanocide.

Farmers have poor administration techniques. This effectively results in under-dosage, fostering resistance.

6.3.9. Supportive care

Farmers give some supportive care — special feeding and worming — however, they are not aware of supportive therapies for anaemia or dehydration.

Farmers should provide more supportive treatment.

6.3.10. Treatment monitoring and response to treatment failure

Farmers use the same diagnostic tools to monitor response as they use for diagnosis. If treatment fails, farmers may repeat the treatment, try another treatment, seek advice or sell/slaughter the animal. They usually do not increase the dosage, but this is standard practice by veterinary agents. Farmers are not aware of drug resistance as a reason for treatment failure.

Farmers monitoring of treatment response is good, but lack of knowledge on drug resistance may lead to inappropriate actions.
Box 3: Problems resulting from improper injections by farmers

- Abscess from unsterile injection in the wrong site, one litre of pus was removed after incision.
- Swollen and infected muscle resulting from unsterile injection; this animal was lame and had lymphadenopathy as a result of the injection.
- Swelling and inflammation resulting from incorrect injections - two of these animals were diagnosed as still being sick with trypanosomosis despite these treatments, indicating the treatments as well as causing side-effects were not effective.
- Spillage of trypanocide due to failure to apply pressure on withdrawing needle and wrong site.
- Subcutaneous pooling of trypanocide due to shallow injection and wrong site.
In summary it can be seen that farmers’ animal-health care behaviour is largely rational, and probably does not unnecessarily promote resistance. There are few major problems in the following important areas:

1. Identification of animals in need of treatment
2. Presumptive diagnosis of trypanosomosis
3. Decision to treat
4. Choice of an appropriate treatment
5. Obtaining the treatment from an appropriate source

The most important fail-points in rational drug use are:

1. Poor differential diagnosis
2. Improper preparation of medicines
3. Inadequate estimation of weight and dosages (but farmers over-dose, which will not foster resistance)
4. Poor injection technique
5. Poor quality control by drug manufacturers.

A possible additional fail-point is the scant use of the alternatives to trypanocides, in particular the alternative of vector control. While technically effective, it is not clear that this vector control is cost-effective at present levels of resistance. However, imperfect understanding of the benefits and mode of action of vector control may also contribute to poor uptake and sustainability. (For example, farmers are unaware that tsetse are the only cause of trypanosomosis; that vector control protects areas rather than individual animals; that vector control can be downscaled after initial high levels, but must continue; that trypanocides are not needed if vectors are not present etc. For a fuller discussion on the reasons for failure of sustainability and uptake of vector control, see Working Paper 2 in this series.)

6.3b. Understanding fail points in Rational Drug Use

The fail points of drug use are primarily related to information availability; farmers lack the knowledge and skills they need to safely and accurately give treatments. Unsafe, unnecessary and inaccurate treatments waste resources, and lead to treatment failure and drug resistance. Underlying these information failures are policy failures:

- Most fundamentally, policy does not take into account the costs and benefits of trypanocide use and the externality of drug resistance, with the result that current policy frameworks do not maximise welfare across stakeholder groups. The interests of stakeholders with high influence and lobbying power prevail over those with less voice, organisation and influence. Further information is needed on costs, benefits and the distribution of these costs and benefits, but enough is known to warrant reconsideration of the current policy framework which determines the provision of trypanocides and services.
- Policy assumes that all trypanocides will be given by veterinary professionals. However, this western-derived model may be logistically unworkable and economically unsound in developing countries. Given that in hyper-endemic areas (much of the cotton zone), the majority of animals require repeated treatments for trypanosomosis, there are insufficient veterinarians to treat individual animals. It is also economically inappropriate, in that farmers cannot afford veterinary fees and are not willing to pay specialists to carry out activities they routinely do themselves. Professional monopoly may also be unjustified from a veterinary health perspective – numerous studies on Community Animal Health have shown that farmers are competent to diagnose and treat simple and common problems. In many countries (including East Africa, USA and UK), farmers carry out routine treatments, including injection of animals, themselves, and legitimisation of farmer treatment could be a necessary and important step forward for Kenedougou. Farmer use of antimicrobials is often objected to because it may lead to residues and resistance with adverse consequences for human health. However, neither of these prob-

3 Resistance is a function of usage, and use of anti-microbials inevitably leads to resistance. Unnecessary resistance occurs when the costs of using the anti-microbial (including externalities) are higher than the benefits of using the anti-microbial.
lems applies to the most widely used trypanocides –residues in food are not considered to
represent serious health risks, and trypanocide drugs for treating cattle are not widely used in
human medicine. Recognising that farmers have a role in trypanocide use is a prerequisite to
better conceptualising this role and removing the barriers that prevent them from adequately
carrying it out.

• Policy assumes that all trypanocides are sold by professionals who provide quality advice and
service. In practice, there are many non-professional actors who also sell drugs, and pro-
fessional actors have quality and service deficits. Recognising the importance of the non-pro-
fessional sector and the deficiencies in the formal sector is the first step towards improving the
way animal health products are delivered.

The study also showed economic incentive failures. Farmers are not able to purchase all the treat-
ments they would like and epidemiological studies indicate they need, because of price con-
straints. Analysis is needed on tariffsication, taxation, mark-up and distribution costs of trypanocides,
but at less than 50 US cents per treatment, the costs are considerably less than those of the same
products in developed countries, and there may not be much scope to further reduce prices.
Reducing prices would increase usage and the impacts of this on resistance would need to be
appraised.

The alternatives to trypanocides (vector control products) are considered too expensive by farmers;
price instruments to decrease costs merit investigation (as vector control provides social as well as
individual benefits, the market price may not be optimal, even assuming a well-functioning
market). However, informational failures also have a role in the failure to use alternatives, and
perhaps more importantly the high transaction costs of forming and maintaining the community
institutions needed to deliver control.

Lack of economic incentives to address market failures have contributed to the narrow range of
trypanocides available, and the scant prospects of more trypanocides being developed.

There are very many regulatory deficits in the sale and use of trypanocides. However, most of
these are part of the wider failure to regulate human and veterinary drugs and are extremely
difficult to resolve. That prescription-only drugs are widely sold by the informal sector and widely
used by farmers, is due not to lack of regulation, but to inability to apply regulation. The therapeu-
tically ideal situation would be that trypanocides are given only by veterinary professionals,
after a clinical examination, confirmed by laboratory tests. This report argues that this is not
logistically possible in the context of Kenedougou, and given present economic conditions and
farming systems, the costs of the therapeutic ideal would far out-weigh the benefits.

6.4. Identifying options and testing best-bet strategies to improve drug use

Given that the central problem in the project area was lack of information on how to use tryp-
anocides, the chosen interventions centred on provision of information. Three different strategies
were selected for evaluation: providing information and training to veterinary professionals, pro-
viding information on drug use to farmers and residential training of farmers in RDU. The third
strategy is taking place in Burkina Faso as part of a community-based integrated trypanosomosis
control project. Other strategies chosen by the farmers in the villages where the project is working
are the use of animal baits and screens to control tsetse. The desired outcomes at farmer level from
the RDU component are given in Box 4. These are based on the guidelines for reducing resistance,
the actual patterns of use in Kenedougou, and the behaviour changes which are feasible given
socio-economic/institutional constraints and resources of the project.

An accompanying workshop report describes the in-depth training of farmers. Evaluation of parti-
cipants before and after the workshop was carried out; this showed significant increase in knowl-
edge, competence and skills as a result of training, and participant evaluation indicated that the
course was highly appreciated. Follow-up training of farmers was given after 10 months and
individual farmers were followed to see if and how knowledge and competencies translated into
behaviour. (Treatments given as well as morbidity and mortality experienced were recorded over the period of one year and compared to non-participants.) However, because multiple strategies for improving trypanosomosis management are being carried out in the four villages, isolating the impact of each component may be difficult. Trypanocides will not eliminate disease and an important part of RDU is the use of alternatives to drugs, where feasible. The project will concentrate on building awareness of vector control and locating competencies for control in the communities – it is by no means certain that this is a sufficiently attractive option given the institutional context of Kenedougou, and at current levels of disease and resistance.

### Box 4: Objectives and messages for farmer training/information provision

**Reduction in quantity of trypanocides unnecessarily used**
- Encourage preventative measures (vector control, good husbandry)
- Use traditional treatments as the first line for mild disease in trypanotolerant animals
- Treat only if a clinical examination and differential diagnosis suggests trypanosomosis
- Avoid block treatments where ISMM resistance is high, or regular treatments not possible
- Use sanative treatments when resistance to only one trypanocide is present
- Include cost-benefit considerations in treatment decisions
- Understand alternatives to trypanocides (vector control, avoidance of high-risk areas, trypanotolerance).

**Proper use of drugs**
- Accurate estimation of dosage (or slight over-dosage)
- Accurate and clean re-constitution of trypanocide
- Good administration techniques (equipment, site, route, technique).

**Increasing the effectiveness of drugs**
- Recognise and treat inter-current infections
- Provide supportive treatment (e.g. nutrition, nursing, fluids)
- Do not delay treatment when diagnosis is clear.

**Monitoring treatment and responding appropriately to drug failure**
- Seek advice (veterinary agent, local expert)
- Reconsider the diagnosis if the animal does not recover
- Provide supportive treatment (e.g. extra feeding, salts, de-worming, ectoparasiticides)
- Sell or slaughter animals who require frequent treatments
- Repeat treatment/change treatment/increase dose (guidelines are lacking for this).

**Sourcing drugs wisely**
- Buy from known and trusted sources who provide quality products and add value with advice
- Recognise and avoid fraudulent, badly stored, date-expired products
- Avoid brands which are more likely to be sub-standard.

**Proper storage and disposal of drugs**
- Store medicines in cool, dark, dry places – traditional ‘refrigerator’
- Store for no longer than indicated by expiry date or manufacturer’s recommendations
- Store in original packets
- Keep safe from children and animals
- Dispose of unused, date-expired medicines
- If medicine containers are used for other purposes, they must first be washed repeatedly.

The strategy of providing information to farmers is being tested in Mali. Information provision is less effective at changing knowledge and practice than in-depth training; however, it is much
cheaper and easier to apply on a wide scale. The strategy of training veterinary professionals is
being tested in Guinea. For this approach to be effective, the formal sector must have a major role
in the provision of services, which is not always the case in sub-Saharan Africa.
7 Broader implications for Rational Trypanocide Use

The problems and constraints identified in this case study are not unique to Kenedougou, Burkina Faso. Similar studies by the project on farmer knowledge and practice in Guinea and Mali revealed similar problems. The issues of inappropriate and unenforced regulation, a large and low-quality informal sector, most treatments carried out by non-professionals and limited skills and knowledge of drug sellers and users are common not only to most developing country animal health sectors, but also to the human health sector. And it is in human health that most work has been done on understanding and improving drug use. Though relevant, the results of these studies are not directly applicable to veterinary drug use, and strategies have to be developed that reflect the particular needs and context of animal health provisions. Given this context, the problems with drug use most widely identified, and the interventions which have proven most successful, most promising avenues can be suggested as follows:

Educational/informational interventions targeting:

- **Livestock keepers.** Farmers are already giving the majority of treatments, and have the highest incentives to do so correctly and cost-effectively, and targeting information at farmers is a potential strategy. Many studies have found that, given small amounts of training and information, farmers can competently give treatments (including injections). Moreover, training improves animal health knowledge and behaviour and often results in positive impacts on livestock health and production. However, in most cases, changes are needed to the existing policy framework before this strategy can be used. Given an enabling policy environment, there are many possible channels for providing information to farmers. The manufacturers of trypanocides have an interest in ensuring that their products are properly used, and could distribute information at very little cost; the same is true for sellers of veterinary products (but not necessarily for sellers of veterinary services, whose interests may be best served by restricting access to information). More objective information could be provided through Farmer Field Schools, which have been very successful at improving the use of pesticides by farmers.

- **Farmer specialists.** (For example, community experts, vaccinators, livestock-rich farmers.) Quantity of use is an important determinant of resistance, and concentrating resources on high-level users may be an efficient way to improve quality of use and combat resistance. In most communities, local experts are sources of advice and treatment as well as acting as role models, so training these will have multiplier effects. Training community-selected farmers as Community Animal Health Workers, who provide animal health services, has been a widely used and largely successful strategy. However, the creation of low-level cadres has been very controversial, with strong opposition from private veterinarians.

- **Drug sellers.** Providing information and/or training to the sellers of trypanocides will also have multiplier effects. Moreover, interventions which address both supply and demand are often more successful than those looking at just one side of the equation. Although quantitative analysis of the relative importance of different service providers has not been carried out, it seems informal sector service providers have a significant role. Informal-sector drug sellers are much more difficult to reach than formal-sector providers. However, they have greater needs for information.

- **Veterinary professionals.** In human health, educational/informational strategies for improving drug use have mainly focused on health professionals, often with good success. Multi-session, multi-method, participatory, practical, problem-oriented methods have been shown to be effective ways of increasing knowledge and changing behaviour. In animal health, professionals are relatively less important in service provision, but in terms of influencing policy, this sector is key. Most veterinary professionals are unaware of the phenomenon of drug resistance, the levels of drug resistance in different areas and the guidelines for trypanosomosis control in the presence of trypanocide resistance.

Managerial interventions to put in place:

**Standards of practice for informal and formal-sector providers.** Targeting interventions at the point of sale rather than point of use has obvious advantages in terms of large-scale outreach, multiplier effects and reducing costs. Farmers have high incentives to give drugs correctly and
ongoing work indicates they are also highly motivated to treat correctly, but their needs for advice and information are largely going unmet. Drug-sellers also have incentives to ensure the remedies they sell, work; for them, giving advice and information can be a value-adding service that improves their competitiveness at little additional cost. Managerial interventions which could be used include prescription guidelines, audit, standard treatments, packaging standards, and performance targets.

Regulatory and economic interventions

As emphasised in this report, regulation and policy failures underlie many informational and managerial failures. They also contribute to lack of effective quality control of trypanocides and to the persistence of market failures that have negative consequences for choice, quality and price of products and services. Unfortunately, these problems have proven very difficult to resolve. The most important fixable regulation failure seems to be poor manufacturing quality control, resulting in a significant number of products with insufficient amounts of active ingredient. For trypanocides, quality is assured not by the seller, but by the manufacturer. Farmers assess product quality by brands, appearance, physical characteristics and conditions of storage, not by the qualifications or legality of the seller. (This seems a rational approach as professionals and non-professionals sell identical products, all of which are imported from outside Africa.) As there are few manufacturers of trypanocides, and many of these are in OECD countries with well-developed regulatory systems, it would be easy for developing country governments to request quality assurance at source, before importing products.
Drug use by farmers is the only innovation for trypanosomosis control which has proved unequivocally viable, self-propagating and capable of auto-financing. In contra-distinction to donor-promoted control strategies, it is used in all communities with significant risk of trypanosomosis, and largely without external support. However, this strategy is increasingly jeopardised by the emergence of resistance to trypanocides. RDU principles, including the promotion where appropriate of alternatives to trypanocides, can improve the effectiveness of current practice and safeguard future use. RDU requires optimising both quality and quantity of use; to meet these objectives, farmers and informal-sector sellers are the most important target groups. But up to now, their involvement has been largely unacknowledged, as policy pursues the ideal that all human and animal treatments are given by trained and qualified professionals. The best is the enemy of the good, and in the real world of economic and institutional constraints, the ‘second-best solution’ of empowering communities to better meet their animal health needs in ways that minimise negative externalities, may be a better bet. Participatory, interactive training is an effective way of doing this but the costs are high, and ‘stroke of the pen’ regulatory and policy reforms to achieve the same goal through removing information barriers, market imperfections and other system constraints need also to be investigated and appraised.
End notes and references


FDA. 1998. CVM concerns about antimicrobial use in food animals. FDA Veterinarian Newsletter. 13:4. Food and Drug Administration, USA.


Heffernan, C Misturelli, F. 2000. The delivery of veterinary services to the poor. Report of DFID project R7359. Veterinary Epidemiology and Economics Research Unit, University of Reading, UK.


Fox, RG, Mmbando, S, Fox, M, Wilson, A. 1993. Effect on herd health and productivity of controlling tsetse and trypanosomosis by applying deltamethrin to cattle. Tropical Animal Health and Production. 25, 203-214


Ghibe valley mentioned in Geert and Holmes op. cit. but unreferenced.


Sackett, DL. 1996. Evidence based medicine: what it is and what it isn’t. BMJ; 312 (7023), 13, 71-72


Evidence-based review of 36 interventions in developing countries to improve drug use. Interventions and strategies to improve the use of antimicrobials in developing countries. Management sciences for health, World Health Organization, Geneva, Switzerland.


Evidence-based review of 36 interventions in developing countries to improve drug use. Interventions and strategies to improve the use of antimicrobials in developing countries. Management sciences for health, World Health Organization, Geneva, Switzerland.

Sackett, DL. 1996. Evidence based medicine: what it is and what it isn’t. BMJ; 312 (7023), 13, 71-72


With modifications from: NHS Centre for Reviews and Dissemination 1996. Undertaking systematic reviews of research on effectiveness (CRD report 4), University of York, York.


Ross-Degnan, D. 1996. The impact of face-to-face educational outreach on diarrhoea treatment in pharmacies. Health Policy and Planning. 11:308-18. This also showed major discrepancies at baseline between reported and observed behaviour indicating attitude and practice deficits rather than knowledge deficits.


Quality studies in Kenya, Cameroon, Chad, Madagascar, Myanmar, Punjab, Vietnam, Pakistan and Lao, found an average of 20% (range 4 to 55, median 16%) were substandard. Reported in Effective Drug Regulation: what can countries do, 1999, World Health Organization, Geneva, Switzerland.


