The View of the Industry on Approaches to the Management of Parasite Resistance

R.J. Curtis and H.-D. Hamel***

* *Intervet GmbH, Wiesbaden, Germany*
** *BAYER AG, Business Group Animal Health, Leverkusen, Germany*

The Veterinary Parasite Resistance Group (VPRG) was formed in 1995 and is an international intercompany body which consists of representatives of nine major companies that research, develop and market antiparasitic and other products worldwide (Bayer, Elanco, Fort-Dodge, Intervet, Merial, Novartis, Pfizer, Schering-Pfizer, Schering-Plough, Virbac).

As an expert consultative group to the Confédération Mondiale de l'Industrie de la Santé Animale – COMISA its role is to advise or direct industry and non-industry on the implications and consequences of parasite resistance, monitoring and management. This is a clear example that the Animal Health Industry is committed to working together to monitor and react to parasite resistance.

COMISA is the global federation representing manufacturers of veterinary medicines, vaccines and other animal health products in both developed and developing countries across five continents.

Its goal is a harmonised, science-based regulatory and trade framework that supports an economically viable and high-technology driven global animal health industry which is contributing to a healthy and safe food supply.

As an international organisation its mission is:

- To speak for the industry with the major international bodies whose involvement with animal health, impacts on the animal health industry. FAO, WHO and WTO are typical examples.

⇒ To help work towards the development of regulatory processes and standards which are both science-based and have an element of certainty about them.

⇒ To represent the industry on a worldwide unanimous basis on dialogue with governments, food industry partners and the consumer.

⇒ To help towards achieving international harmonisation of regulatory and registrations requirements.

Within its affilation to COMISA the VPRG-COMISA functions to

⇒ Ensure the establishment of appropriate lines of communication to make certain that parasite resistance management strategies and the associated rationale for

these are transferred accurately to the implementation level of the relevant bodies.

⇒ Provide clear and well supported advice on actions to be taken (and the consequences of "non-action") directly to national and international authorities/decision makers/advisers on all aspects of parasite resistance.

⇒ Coordinate within industry ways of prolonging the effective life of veterinary parasiticides by defining, recommending and monitoring technically sound strategies for parasite control and maintaining an up-to-date awareness of resistance problems.

The VPRG-COMISA has established and continues to update a series of databases [see below], primarily from the published literature supported by pooled information from in-country sources, on the international situation on resistance, in ticks (cattle), *Psoroptes ovis* mange mites (sheep), *Haemonchus contortus* (sheep), *Trichostrongylus colubriformis* (sheep), *T. axei* (cattle), *Ostertagia ostertagi* (sheep), Cyathostomes (horse).

The status of resistance in these organisms is well known and for example that of *Boophilus microplus,* in Australia, given below, is probably the most well researched in terms of resistance to a succession of acaricides of the same and differing chemical groups.

Table 1:

Chemical	Year	References
Arsenic:	1936	Wharton (1976)
DDT:	1953	Wharton (1976)
Toxaphene-BHC-dieldrin group:	1953	Wharton (1976)
Organophosphates:	1963	Wharton (1976)
Amidine:	1980	Nolan (1981)
Pyrethroid [predicted]:	1979	Nolan et al. (1977)
Pyrethroid [reported]:	1989	Nolan et al. (1989)

Similarly the chronological evolution of resistance in Horn fly [*Haematobia irritans*] in the USA from 1945 to the mid 1980s from DDT to the synthetic pyrethroids has been reviewed by Sparks et al (1985).

Information of progressive resistance to anthelmintics with some chronology was reviewed by Kelly & Hall (1979a, 1979b) and Pritchard et al (1980) and more recently by by Dobson et al (1996) and Sangster (1999).

Prior to the formation of the Group all companies pursued their own parasite culture requirements and test methods. In many cases data obtained were not compatible and could have possibly led to misinterpretation of the level of susceptibility of the parasite under examination. With the formation of the Group all existing information on laboratory strains and test methods were pooled and are available within and to the Group as a whole.

Within the test systems for ticks, the Yeerongpilly strain of *Boophilus microplus* was the internationally accepted susceptible strain against which all resistance testing was done by the Industry and the first-step towards research screening for new acaricides.

All the databases compiled by the Group were passed on to FAO, with which industry collaborates, via the VPRG-COMISA, as members of the FAO/Industry Group on Parasite Resistance. FAO in turn produced additional in-country data on all major ecto- and endoparasite resistance forms, a worldwide survey to provide the first international survey of this type (Nari and Hansen, 1999).

Clearly, all test systems used in the past by the Animal Health Industry, Universities and institutes all served a specific purpose. However, as parasite resistance, particularly in some genera, has become both more widespread and complex, this stimulated the need to examine the resistance of parasites to commercially available active ingredients in a more controlled and critical manner. This led to the initiation of the concept, within industry and FAO, of standardisation of resistance testing from the field to reporting. Clearly this step provides a beneficial tool to all concerned with parasite resistance monitoring and research. It also provides a uniform basis for comparisons between strains and within and between chemical groups.

First steps have already been taken in *Boophilus* ticks, using the tick larval packet test and the adult immersion test, the majority of the work being done by Drs. Kemp and Thullner as members of the FAO/Industry Group and the FAO/Industry Contact Group on Parasite Resistance and consultants to FAO. The larval dispersal test for amidine resistance has been added to the test portfolio. Statistical analysis of test results and supply of actives still need to be addressed.

Coles et al (1992) have provided test systems to assess resistance to anthelmintic compounds but no tests have yet been devised and standardised for nematode resistance to macrocyclic lactones.

Approaches to a form of standardisation of testing for resistance in *Haematobia* spp , particularly to synthetic pyrethroids, have been made in the USA latterly using larvae as the indicator stage e.g. Crosby et al (1991), which followed on from the earlier developed test systems for field caught adults at the University of Georgia by Sheppard and Hinkle (1987) and the Universities of Lousiana and New Mexico by Byford et al. (1985). The method established several years ago for testing compounds against and for resistance in *Lucilia cuprina* was used to evaluate the possibilty of cross resistance in this organism to synthetic pyrethroids following extensive use of these compounds against lice on sheep.

The reach of the VPRG internationally is very expansive with over 500 separate subsidiary companies. Each has competent technical representation available to channel information into the Group regarding parasite resistance down to farmer level (see schematic on communication route). In general in the Industry it is the local company that is the first line of information on possible field problems based on monitoring and complaint investigation. This results in a flow of information into the Group as required but in the majority the concerns on resistance are unfounded and resolved on the spot by providing and applying appropriate and correct parasite management by local technical personnel. Whilst correct technical advice is offered

at farmer level and awareness is created e.g. at farmer meetings, should a problem arise which is thought to indicate resistance then the on-farm status of all parasites would be double-checked by re-treatment.

Additionally, parasites in the surrounding area may be also checked. Immediate advice would be offered on the use of alternative chemical groups and a strategy devised, making sure substituted products are used correctly. This applies most importantly to new products based on novel chemicals.

One of the major problems within parasite control and combating resistance is the continued appearance on the market in certain areas of products which do not appear to have a regulatory package up to accepted international standards.

Thus in those cases when resistance is confirmed the VPRG-COMISA can recommend actions to be followed but success would be highly dependent on the cooperation of all companies, marketing products containing the active in question.

As a follow-on to this, at the request of FAO, the VPRG-COMISA prepared and supplied this organisation with what could be considered as the minimum registration requirements for the registration of an antiparasitic product. However, how this will be communicated, followed-up and how successful it will be in countries which appear to need such guidance, remains to be seen.

There is a role for education in minimising the possiblity of resistance occuring but it is accepted that it can never be totally eliminated. However, every effort is made in this direction to extend the useful life of antiparasitic compounds. Although many farmers are fully informed and very aware of parasite resistance and the consequences of this, there is a high dependence upon the receptiveness, of those concerned, to literature and verbal advice offered by the industry. This emphasises the role of the various intermediaries and the responsibility that these are fully informed of the company strategy. The company in turn has to monitor carefully the marketing process.

Delaying parasite resistance is important to the industry as it is committed to protect what is currently a limited resource, particularly with regard to tick control which has been severely jeopardised in the past and could be in the future. This also has to be appreciated by those in the hierachy between the company and the farmer.

Thus resistance monitoring and control has to be considered a priority and the establishment by FAO of the first Acaricide Resistance Reference Centre in Mexico has to be considered a positive step. These will follow agreed standardised procedures for testing for resistance in ticks. At the time of preparing this presentation the Industry sees these centres performing the following functions within their terms of reference in each country/geographical region.

A Regional Centre would be responsible for:

- data-banks,
- culture and definition of the profile of the standard susceptible and resistant strains of *Boophilus* spp,
- prepare and distribute test papers,

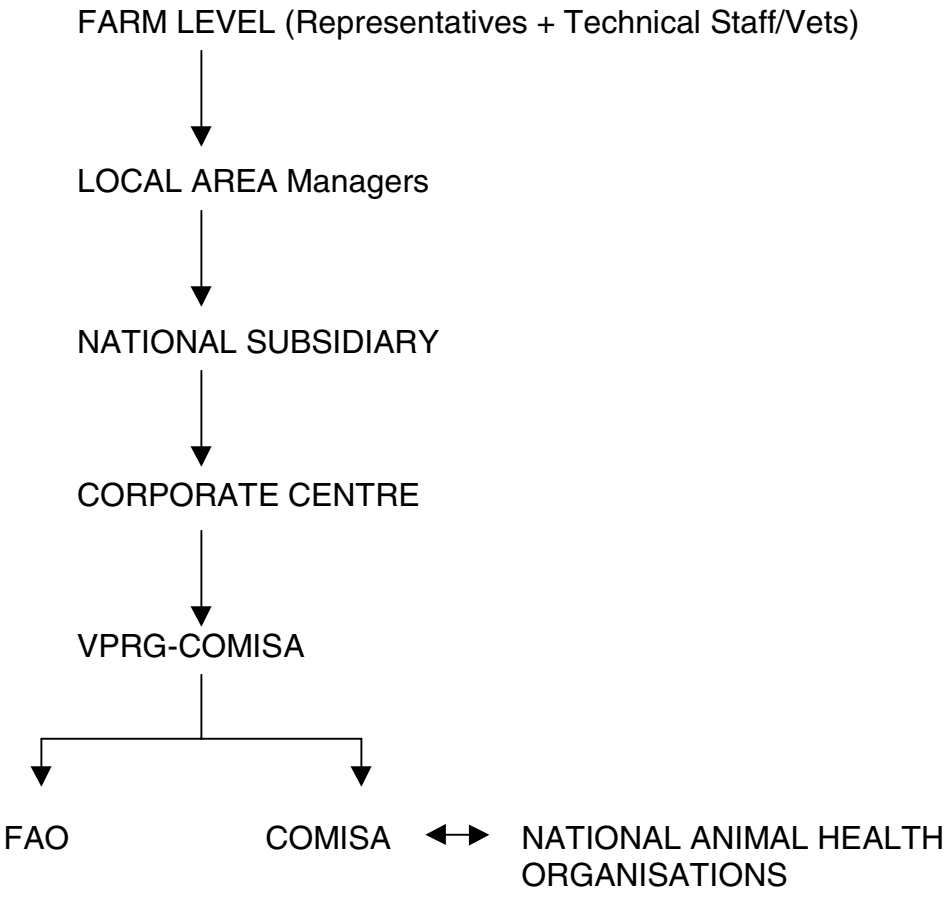
- carry out specialist testing on unique resistant strains to type these as they are isolated,
- define and control further actions down-the-line,
- act in an advisory function.

A Country Centre would be responsible for:
- interfacing with the Regional and Local Centres,
- data-banks
- propagate agreed actions,
- advisory.

A Local In-country Centres would be responsible for:
- interfacing with the Country Centre,
- data banks,
- typing local strains,
- unique testing if within capabilities,
- local advice,
- instigating further actions.

Table 2:

Infrastructure available to the VPRG-COMISA worldwide to monitor parasite resistance



Thus FAO and the Industry together are looking in depth at resistance in livestock parasites and at ways of delaying this. This involves standardisation of procedures so that there can be no conflict in interpretation. It may also involve factors other than chemical control in the strategies derived.

REFERENCES

Byford RL, Quisenberry, SS, Sparks TC and Lookwood JA (1985). Spectrum of pesticide resistance in pyrethroid resistant populations of Haematobia irritans (L). J. Econ Entomol .78: 768-773.

Coles G C , Bauer C, Borgsteede F H, Geerts S, Klei T P, Taylor M A and Waller P J (1992). World Association for the Advancement of Veterinary Parasitology (W.A.A.V.P.) methods for detection of anthelmintic resistance in nematodes of veterinary importance. Vet Parasitol. 44: 35-44

Crosby B L , Byford R L and Sparks T C (1991). Bioassay for detecting active site insensitivity in Horn fly (Diptera:Muscidae) larvae. J Econ.Entomol 84: 367-370

Dobson R J , LeJambre L and Gill J H (1996). Management of anthelmintic resistance: Inheritance of resistance and selection with persistent drugs. Int. J. Parasitol. 26: 993-1000

Kelly J D and Hall C A (1979a). Anthelmintic resistance in nematodes. History, present status in Australia genetic background and methods for field diagnosis. NSW Proc 15: 19-32 ARMANDO NEEDS TO CHECK THIS TITLE AS IT IS A REFERENCE HE HAS USED

Kelly J D and Hall C A (1979b) Resistance of animal helminths to anthelmintics. Adv. Pharmacol. Chemother. 16: 89-128

Nari A and Hansen J W (1999) Resistance of ecto- and endoparasites: current and future solutions. 67th General Session: International Committee. OIE. Paris, 17-21 May 1999.

Nolan J Roulston, W J and Wharton R H (1977). Resistance to synthetic pyrethroids in a DDT-resistant strain of Boophilus microplus. Pesticide Science 8: 484-486

Nolan J, Roulston W J and Schnitzerling H J (1979). The potential of some synthetic pyrethroids for the control of the cattle tick (Boophilus microplus). Aust. Vet. J. 55: 463-466

Nolan J. (1981). Current developments in resistance to amidine and pyrethroid tickicides in Australia. Tick Biology and Control, Proceedings of an International Conference 27-29 January 1981, 109-114. Ed. G B Whitehead and J D Gibson

Nolan J., Wilson J.T., Green P.E. and Bird P. E. (1989). Synthetic pyrethroid resistance in field samples in the cattle tick. Aust. Vet. J., 66: 170-182

Prichard R K , Hall C A Kelly J D Martin I C and Donald A D (1980). The problem of anthelmintic resistance in nematodes. Aust, Vet. J. 56: 239-251

Sales N, Levot G W and Hughes P B (1989) Monitoring and selection of resistance to pyrethroids in the Australian sheep blowfly, Lucilia cuprina. Med. Vet. Entomol. 3: 287-291

Sangster N C (1999) Anthelmintic resistance: past, present and future. Int. J. Parasitol. 29: 115-124

Sheppard DC and Hinkle NC (1987). A procedure using disposable material to evaluate horn fly insecticide resistance. J. Agric. Entomoml. 4: 86 – 89.

Sparks T C, Quisenbury S S, Lockwood J A, Byford R L and Roush R T (1985). Insecticide resistance in the Horn fly Haematobia irritans. J. Agric. Entomol. 2: 217-233.

Wharton R.H (1976) Tick-borne Livestock Diseases and their Vectors. 5. Acaricide Resistance and alternative methods of tick control. Wld Anim Rev 20: 8-15.