STUDY PROTOCOL

„Clinical Study on the efficacy of the preparation labelled CV 247 on pet dogs affected with malignant neoplasia"

Non-commercial Phase II/a clinical study.

date: 11 March 2008

Study Co-ordinator: Andor Sebestény D.V.M., B.V.Sc., Dip.Bact., MRCVS

History:

Preparation CV 247 has been on clinical trial in Great Britain for the past two decades on dogs suffering from malignant neoplasia. Results showed an improvement in the general condition of most of the treated dogs and in a smaller proportion of cases antitumour effect has also been observed. The use of the preparation appeared to promote the regression or at least impede the progression and spread of some histologically identified malignant tumours and slow down or even prevent the predicted regrowth and/or metastasis of some surgically removed malignant tumours.

The CV 247 preparation is also being tested in human patients in Great Britain. It appears to be effective or the basis of results so far in patients suffering from prostatic cancer.

The Initiators and Executors of the study:

Sponsor: IVY Medical Chemicals Development Ltd.

Organisers and Participants of the clinical study:
Dr. Zita Kósa
Dr. Zsolt Sebestyén

Pathological examinations:

Dr. Mihály Albert

Statistical analysis:

Ibolya Nyárádi

Sites of the study:

1025 Budapest, Csévi u. 1.

1082 Budapest, Horváth M. tér 11.

Data may be provided to the above study sites by all veterinary practices and clinics which are able to fullfill the criteria of the study and undertake the full adherence to the Study Protocol. They will have to declare which of the above test sites they wish to be associated with at the outset.

Pathological examinations may be carried out by any specialist beside the ones named above.

The aim of the study:

The gathering of evidence on the efficacy of Preparation CV 247 in dogs suffering from inoperable and/or metastising malignant tumours which would not respond to other therapies, or the already removed tumour has regrown or the chances of this is high according to data in the literature.

The study seeks answer to the question whether CV 247 applied as an adjuvant therapy proves to be effective, i.e. **primarily** whether it reliably improves the well-being and quality of life, and **secondarily** whether it also may decrease the rate of growth and spread of the malignant tumour or the chances of the expected regrowth of the malignant tumour.

Preparation under Study: CV 247.

Manufacturer: Pharmaserve Ltd.

Presentation: CV 247 contains four ingredients in distilled water: Sodium salicylate, Ascorbic acid, Manganese gluconate and Copper gluconate. One "Unit Volume" of 10 ml of CV 247 mixture will contain :

Ingredient	**Pharmacopoeial Status**	**Unit Volume (Per 10 ml)**
Ascorbic acid	Ph Eur	400.0 mg (4%)
Sodium salicylate	Ph Eur	350.0 mg (3.5%)
Manganese gluconate	USP	20.0 mg (0,2%)
Copper gluconate	USP	20.0 mg (0.2%)

Storage:

Sodium salicylate, Manganese gluconate and Copper gluconate are presented as a base solution in 300 ml bottles which may be stored at 2-8 C unopened for 18 months.

Once it is mixed with Ascorbic acid, it may be kept for 1 week only at 4 C.

Dosage:

A measured amount of 400 mg ascorbic acid powder is to be mixed with 10 ml "Unit Volume" of the solution prior to administration. This 10 ml "Unit Volume" is the maximal dose of this mixture that can be given on one occasion per os. The dose calculated on body weight basis according to the table below should be administered **twice a day before feeding**:

< 7 kg	**7-14 kg**	**14-21 kg**	**21-28 kg**	**28-35 kg**	**>35 kg**
1.5 ml	3.0 ml	4.5 ml	6.0 ml	7.5 ml	9.0 ml

(The preparation is administered by the owner of the dog either directly into the mouth, or mixed into a small amount of the dog's favourite food or drink so that it would be consumed without fail.)

A change of diet is an integral part of CV 247 treatment. (It should be rich in green and root vegetables, vitamins and fibre and should contain liver and fish as protein source).

Period of study:

Observation for **6 months** from the date of commencement of the treatment with CV 247.

(Optional follow up thereafter with possible further examinations, tests and communications with the owner, similarly to the earlier British studies.)

Dogs to be admitted for study (age, sex, numbers):

Dogs suffering from malignant tumours which are not suitable for surgery or have already metastasized, or have regrown after surgery, or the owner declines surgery or conventional radio- or chemotherapy from the outset.

Numbers in one group : **minimum 20 dogs** per type of tumour.
Dogs of *mixed sexes* to be mostly above 5 years of age.
Age groups: 5-8 years, 9-11 years, 12 years or above.

Control cases:

The case histories of dogs with comparable malignant tumours treated either by conventional means or by other types of adjuvant therapies will be submitted with the owners consent. In addition, historical data from the literature on the survival rates, regrowth and metastastis rates of comparable malignant tumours in dogs will be given.

Assessment of efficacy:

An initial biopsy from the tumour is to be taken. The study should concentrate on the most prevalent types of malignant tumours: **mastocytoma, mammary carcinoma, malignant melanoma and B-cell lymphoma.**
Before the commencement of the therapy other concurrent conditions should be excluded (chronic fibrotic hepatitis or nephritis, chronic decompensated cardiac conditions, advanced Cushing disease, diabetes mellitus etc), as their presence excludes the subjects from the study. Dogs already receiving chemo- or radiotherapy should also be excluded from the study.

The tumour already diagnosed and typed should also be subjected to the determination of its TNM stage by detailed diagnostic tests.
The detailed history and present clinical state of the dogs under study are to be recorded.
The commencement of the administration of CV 247 treatment followed by regular clinical examinations including:

The measurement of the size of tumours and lymph nodes.

The observation of metastases.

Measuring body weight. This should be taken before treatment commences and fortnightly thereafter.

Assessment of the quality of life of the treated dog:

The **veterinarian administering the treatment assesses fortnightly**, while the **owner assesses weekly** the quality of life and makes a dated recording using the grades below:

1. Very poor, not eating or drinking, hunched, nearly moribund.
2. Poor, hardly eating and moving.
3. Poorer than average, little appetite, does not want to go out.
4. Average, not healthy looking, depressed but is eating and goes out briefly.
5. Average with good appetite, but rests and sleeps more than usual.
6. Livelier than average, with good appetite and is willing to go out.
7. Very lively with voracious appetite and vigour, demands to go out.
8. Quality of life is better than before the illness started.

Assessment of tumour progression or regression:

Surface tumours to be measured fortnightly by callipers. Measurements should be taken at the two widest dimensions. On irregularly shaped tumours at least 3 measurements will be needed from which a mean value could derived.

Deep seated tumours will require other means (X-ray, ultrasound or tomography) for taking measurements as above.

Pathological examination: At the outset the owner should give an undertaking to allow the postmortem examination of the treated animal, should it die for any reason. Antitumour effect can be classed within 5 categories:

1/ Regression

2/ Stabilization

3/ Progression

4/ Local spread

5/ Metastatic spread

Dogs lost during the study should be subjected to pathological examination preferably within facilities suitable for this and samples should be taken from the tumours found.

(If the transport of the body to a pathology laboratory is impractical, the veterinarian has to perform an autopsy and record the findings, possibly including informative photographs and take descriptively labelled samples for histology from the primary and secondary tumours. These should be sent without delay to the pathologist monitoring the case).

Treated animals after the study period should be subjected to clinical examination, laboratory tests and possibly biopsy for histopathology.

Data after evaluation should be subjected to statistical analysis as to their significance.

The efficacy of the treatment

The preparation will be considered effective if the quality of life of the treated animal as judged by the regular clinical examinations and by the owner's own assessment reports improves inspite of being affected with a malignant neoplastic condition. (i.e. no loss in body-weight and the well-being of the animal improves significantly).

It will be considered to be even more effective if during the observation period the malignant tumour does not increase, or possibly reduces in size and the number of metastases do not increase or possibly decreases in number, and thereby the life expectancy increases.

Statistics:

The analysis of the normal distribution of data. The application of the ANOVA test in case of homogeneous data, and of the Krustal-Wallis ANOVA test in case of inhomogenous data. In case of a significant variation ($p<0.05$), the use of appropriate post-hoc test for the analysis of data.

The changes in body weights, in the quality of life reports returned by the veterinarians and by the owners, and in the tumour sizes will be the subjects to statistical analysis.

Reporting:.

Following the conclusion of the study (at the finish of the observation period of the last patient) within 2 months all raw data will be collected from the 3 study sites (and from any other affiliated sites) and will be collated for the Study Organiser. During the study period an interim report on 10 animals per treatment group will also be given to him.

The deadline for the presentation of the draft report: **the end of the 5th month following the conclusion of the study.**
The deadline for the presentation of the final report: **30 days from the approval of the draft report.**
All raw data, return sheets and examination reports will be collected after the final scrutiny and returned to the Sponsor.

SIGNATURE(S)

The clinical efficacy study of preparation "CV 247" in dogs affected with malignant tumours.

Non-commercial II/a Phase clinical study

Version No: 2.0 date: 11 January 2008.

I will conduct the study according to the Protocol

…… …….

signature date

…….

Name printed

(Should be signed by all persons participating in the study).

Annexes:

1. Receipt Forms for the preparation
2. Forms for the return of unused preparation and containers
3. Owner's information sheet
4. Owner's Form of Consent
5. Owner's Quality of Life Assessment Forms
6. Pathology Report Form
7. Histopathology Report Form
8. Undertaking from clinical study collaborating sites
9 Clinical Examination Report Forms
10 The professional CV of the Principals of the 3 licenced clinical study sites

Annexe No 1

The clinical efficacy study of preparation "CV 247" in dogs affected with malignant tumours.

Receipt Form for Preparation CV 247

I have received Solution CV 247 for use.

Amount:……...
Date of Manufacture:
Serial No:
Expiry Date:

Data of the User:

Name:……

Clinical Study Site: ……...

……..

Signature:…….

Data of Provider:

Name: …….
.
Source:……

Signature:…….

Date: …….

Annexe No 2:

The clinical efficacy study of preparation "CV 247" in dogs affected with malignant tumours.

Transfer-Receipt Form for Preparation CV 247
(For expired, unused preparation or empty containers of used CV 247)

-For the return of unused containers of CV 247 Solution and Ascorbic acid powder*

-For the return of expired CV 247 *

-For the return of unused CV 247*

Amount:……...
Date of Manufacture:
Serial No:
Expiry Date:

(* to be underlined)

Data of Recipient:

Name:…….

Clinical Study site:…….

…… Signature:…….

Data of Returning User:

Name: …….
.
Source :……

Signature:……

Date: ……..

Annexe No 3

The clinical efficacy study of preparation "CV 247" in dogs affected with malignant tumours.

Owner's Information Sheet

Dear Pet Owner,

With your consent a new preparation will be given to you for oral administration to your dog suffering from cancer, which has been shown on studies already carried out to be safe and free from side-effects, while it should improve **the well-being and quality of life and possibly also the life expectancy of your dog.**

The present study is necessary for the registration and manufacture of the CV 247 preparation for supplementary (adjuvant) therapy of cancer cases.

In earlier studies carried out on dogs in Britain it has been also observed in some patients treated with CV 247 that the malignant tumour has shown signs of regression.

We are looking for answers in this study whether the preparation CV 247 has a sufficient efficacy in dogs affected with certain cancers in the improvement of their well-being and perhaps also the size, growth rate, or chances of the regrowth of already removed tumours are diminished after treatment.

The planned period of treatment is 6 months. During this you will receive regularly the Preparation CV 247 free of charge from you veterinary surgeon who will give you written instructions as to its use.

Your task is to store and administer to your dog the CV 247 Preparation according to the instructions. Also, during the treatment period every week, preferably at the same times of day, observe and assess the dog's behaviour, well-being and quality of life and record it on the forms provided. Futhermore, during the treatment make an appointment with your veterinarian every fortnight for examination and his assessment of your dog’s progress.

In addition, the feeding of your dog has to be modified. The diet should contain root and green vegetables, fruits (rich in fibre and vitamins) and liver and fish should be the main source of animal protein. The food should not contain preservatives, salt, sugar and colourants. **The amount of feeding should be disciplined.**

Should your dog die during the 6 months' treatment period, postmortem examination has to be carried out as its results may give valuable information for the study. (Arrangements for burial may be made after this examination).

It is the condition of the commencement of CV 247 treatment of your dog that you accept these conditions with your signature of consent.

You may at any time ask for the discontinuation of the treatment from your veterinarian. This will be agreed upon after a final examination and assessment is carried out.

If you do not carry out the tasks you have consented to, such as the correct treatment according to instructions, omitting clinical or pathological examinations, or discontinuing unilaterally the treatment, the Sponsor of the study may require compensation, as he provides the preparation free for your dog and covers the costs for the examinations.

On the other hand, if you satisfy all the requirements of the correct administration of CV 247 and of the recommended diet, of all the monitoring and recording and you submit all the completed records to the veterinarian by the end of the 6 months observation period, all fees taken for the initial examinations and diagnosis before your signing the Consent Form will be refunded to you.

Budapest, January 2008

Annexe No 4

The clinical efficacy study of preparation "CV 247" in dogs affected with malignant tumours.

Owner's Form of Consent

Undersigned……..……

At address……..

Identity Card No…….

I give my consent freely, without any influence, that my dog

Named…….. Breed……..

Age……Sex…….. …….

Identification……

will be treated for 6 months with preparation CV 247 under trial.

I have read and understood the Owners' Information Sheet provided and the instructions from the Veterinary Surgeon.
I will fulfill my obligations regarding the administration of the CV 247 treatment, my providing data and presenting my dog for routine examinations and tests, in order to ensure the success of the treatment and the improvement of my dog's well-being and of its chances of increased life expectancy.

I consent to a postmortem examination should my dog die during the treatment period.

I have been informed that the CV 247 treatment and associated examinations and tests will be given free of charge. In addition, all fees taken for the initial examination and diagnosis before my signing this Consent Form will be refunded to me, if I fully comply with the instructions as to the correct administration of CV 247 and of the recommended diet, of the required recording and veterinary monitoring and of the submission of my records to the monitoring veterinarian.

I acknowledge and accept responsibility for any damages that may occur through my premature unilateral discontinuation of treatment, or omissions of providing data and of presenting my dog for routine examinations or tests.
I understand that the CV 247 treatment may only be prematurely discontinued after informing the veterinarian in charge and after his final examination and tests will have been made.
.
I will use the following registered test site for CV 247 treatment:

1025 Budapest, Chevy u. 1 (Please underline your choice)

1082 Budapest, Horvath M. tar 11.

Name of veterinarian administering treatment: ……

Signed: Date ……..

…….. ……
Owner of the dog Veterinarian providing information

Annexe No 5

The clinical efficacy study of preparation "CV 247" in dogs affected with malignant tumours.

Owner's Quality of Life Assessment Form

Treating Veterinarian:	Test Site:
Serial Number of Case	Name of Pet Owner:
Breed:	Age, Sex (date of neutering if any):
Start of treatment:	Diagnosis:

(Heading to be filled in by the treating veterinarian)

1. Very poor, not eating or drinking, hunched, nearly moribund.
2. Poor, hardly eating and moving.
3. Poorer than average, little appetite, does not want to go out.
4. Average, not healthy looking, depressed but is eating and goes out briefly.
5. Average with good appetite, but rests and sleeps more than usual.
6. Livelier than average, with good appetite and is willing to go out.
7. Very lively with voracious appetite and vigour, demands to go out.
8. Quality of life is better than before the illness started.

Please assess weekly your dog's quality of life weekly according to these grades:

Serial Number	Date of assessment	Grade of quality of life	Treating veterinarian	Serial Number	Date of assessment	Grade of quality of life	Treating veterinarian
1				13			
2				14			
3				15			
4				16			
5				17			
6				18			
7				19			
8				20			
9				21			
10				22			
11				23			
12				24			

Conclusion of treatment period……..

---------- ……

Owner of Pet Veterinarian

Annexe No 6

The clinical efficacy study of preparation "CV 247" in dogs affected with malignant tumours.

Pathology Report Sheet

Treating Veterinarian:	Test Site:
Serial No of Case:	Name of Pet Owner:
Breed:	Age, sex (date of neutering):
Start of Treatment:	Diagnosis:

Date of Death:	**Number of Photos:**
Time of Postmortem:	**Type (CD/DVD etc) and labelling of data carrier:**
Veterinarian performing Autopsy:	**Number of histology samples:**
Diagnosis:	

<u>External Examination</u> (developmental stage, nutritional status, skin, coat, visible mucous membranes, eyes):

<u>Body Weight:</u>

Internal Examination I:

Subcutaneous tissue:

Regional Lymph Nodes:

Blood:

Skeletal musculature:

Internal Examination II:

Abdominal Cavity:

Peritoneum, abdominal contents:

Spleen:

Liver:

Pancreas:

Stomach, gastrointestinal tract (small and large intestines):

Mesenteric Lymph Nodes:

Adrenals:

Urinary tract (kidneys, ureters, blabber, urethra):

Sexual organs and accessory glands (ovaries, oviducts, uterus, vagina):
(testes, epididymis, prostate):

Thorax:

Pleura:

Lungs:

Mediastinal Lymph Nodes:

Thymus:

Heart and great bloodvessels:

Cervical organs and oral cavity:

Tongue:

Pharynx:

Tonsils;

Larynx:

Oesophagus and Trachea:

Thyroid and parathyroid glands:

Nasal Cavity:

Cranium and vertebral column:

Brain, spinal cord, hypophysis:

Bones and joints:

Annexe No 7

The clinical efficacy study of preparation "CV 247" in dogs affected with malignant tumours.

Histopathology Report Form

Treating Veterinarian:	Test Site:
Serial No of Case:	Name of Pet Owner:
Breed:	Age, sex (date of neutering):
Start of Treatment:	Diagnosis:

Date of submission of specimen:	**Date of Report:**
Veterinary Pathologist:	**Number of specimen:**
Diagnosis:	

Origin of specimen:

Macroscopic appearance:

Histological description:

Supplementary Tests: (Differential staining, immunohistochemistry, etc)

Annexe No 8

The clinical efficacy study of preparation "CV 247" in dogs affected with malignant tumours.

STATEMENT

Undersigned: ……

The Principal of the Veterinary Clinic: …….

……..…….

I wish to participate in the efficacy study of Preparation CV 247.

I will carry out the examinations, inform Pet Owners and make Reports according to the Protocol.

I wish to be affiliated with the following Authorised Test Site*:

- 1025 Budapest, Csévi u. 1. (Dr. Sebestyén Zsolt)
- 1082 Budapest, Horváth M. tér 11. (Dr. Kósa Zita)

*Please underline your choice

Date:……

……. …….

Signature Signature of Test Site Principal

Annexe No 9 **Clinical Examination Report**

Name of Veterinarian: Site:

Case Number:	Name of Pet Owner:
Breed:	Age, Sex, (Neutering date):
Start of treatment:	Diagnosis:

Life Quality Grades to use:

1. Very poor, not eating or drinking, hunched, nearly moribund.
2. Poor, hardly eating and moving.
3. Poorer than average, little appetite, does not want to go out.
4. Average, not healthy looking, depressed but is eating and goes out briefly.
5. Average with good appetite, but rests and sleeps more than usual.
6. Livelier than average, with good appetite and is willing to go out.
7. Very lively with voracious appetite and vigour, demands to go out.
8. Quality of life is better than before the illness started.

Date:	Description of tumour (size, shape, consistency):				Life Quality Grade:
	Status present:				
Tests:					
Body Weight:	Lymph Nodes:	Respiration:	Heart, Circulation:	Mucous membranes	Temperature:

Date:	Description of tumour (size, shape, consistency):				Life Quality Grade:
	Status present:				
Tests:					
Body Weight:	Lymph Nodes:	Respiration:	Heart, Circulation:	Mucous membranes	Temperature:

CV 247 test program fee costings

		HUF	GBP
1	**Clinical Examinations**		
	General examination		
	(for initial diagnosis)	6 000	20
	Sampling (biopsy or removed tumour		
	tissue sampling with general anaesthesia,	12 000	40
	laboratory examination (blood, urine etc)	6 000	20
	TOTAL	**24 000**	**80**
2	**Histological examinations**	3 000	10
3	**Further examinations as necessary**		
	(e.g ultrasound) to elminate conditions		
	excluding the patient from the study	8 000	26
	GRAND TOTAL	**35 000**	**106**

These are paid by the Dog Owner, but are refundable to him upon the successfully documented conclusion of the study.

EXAMINATIONS AFTER SIGNING THE CONSENT FORM BY THE OWNER

4	**Initial examinations**		
	Clinical examination	6 000	20
	blood sampling	3 000	10
	blood tests	12 000	40
	X-ray	10 000	33
	Ultrasonics	8 000	26
	TOTAL	**39 000**	**129**
5	**Fortnightly control examinations**	8 000	26
	12 examinations during 6 months		
	with tumour measurements, administration		
	and owner management TOTALLING	96 000	312
6	**Monthly blood tests**	12 000	40
7	**2-monthly special examinatons**		
	(X-ray, ultrasonic)	10 000	33
	3 x TOTALLING	30 000	99
8	**Pathological examinations**		
	Detailed postmortem examination		
	of lost patients including histology sampling,		
	photo-documentations, disposal	25 000	63

9	**Conclusion of the Study at 6 months (Repetition of examinations under 3/)**		
	general physical examination	6 000	20
	blood sampling	3 000	10
	blood tests	12 000	40
	X-ray	10 000	33
	Ultrasonics	8 000	26
	TOTAL	**39 000**	**129**

OPTIONAL FURTHER COSTS BEYOND THE 6 MONTHS STUDY PERIOD

Fortnightly Control exminations	8 000	26
12 examinations with tumour measurements administration and owner management TOTAL	96 000	312
Pathological examinations		
Detailed postmortem examination of lost patients including histology sampling, photo-documentations, disposal	25 000	63

Conclusion of the Study at 12 months (Repetition of examinations under 3/)		
general physical examination	6 000	20
blood sampling	3 000	10
blood tests	12 000	40
X-ray	10 000	33
Ultrasonics	8 000	26
TOTAL	**39 000**	**129**

TASKS FOR THE CLINICAL VETERINARY SURGEON IN THE CV 247 STUDY

1/ Clinical examination followed by sampling for pathological examination in case of suspected malignancy. (If it not submitted to the pathologist named in the Protocol, it should be accompanied with the completed Histology Request Form downloaded from the Protocol).

2/ Clinical examination of the dog to eliminate conditions excluding the dog from the study.

3/ Offering the option of inclusion of the dog in the study to the Owner on the basis of the clinical and pathological results.

4/ On the consent of the Owner the handing over the Owner Information Sheet together with verbal informations as to the details of the study and the tasks of the Owner.

5/ Signing of the Consent form by the Owner

6/ Contacting one of the Test Sites named in the Protocol with a request for a Case Serial Number.

7/ Filling in a Quality of Life Assessement Form for the Owner with verbal instructions as to its use.

8/ Discussion as to the diet of the dog:

9/ Sending in the completed Affiliation Form to the Study Site selected (Possibly by e-mail) for the receipt of the confirmation of enrolment and Case Serial Number allocated.

10/ Sending the signed Affiliation Form to the selected Study Site.

11/ The veterinarian requiring CV 247 arranges its procurement with the Test Site chosen.

12/ Filling in the Transfer/Receipt Forms for all such transactions..

13/ The establishment of the TNM grade of malignancy of the tumour (Clinical laboratory tests, X-ray, ultrasonics, and consultation with Dr Peter Vajdovich at the Budapest Szent Istvan Veterinary University, Dept of Internal Medicine. Tel: 00-36-1-478-4100 Ext.8202).
Note: The fee for the laboratory tests needs to be settled by the veterinarian. The Reports of results have to be attached to the Case Records.

14/ The fortnightly examination and assessment of the patient with taking measurements of palpable tumours. If necessary the Owner of the patient needs to be reminded by telephone of his appointment and of the need to bring with him his weekly Assessment Form.

15/ Monthly blood tests.

16/ Two monthly clinical diagnostic examination (if and as required by the site and nature of the tumour). The number and size of deep seated tumours need to be established.

17/ The entry of data in the Clinical Record Sheets.

18/ Checking and signing the weekly Owner's Assessmernt Forms and their entry into the

clinical Records.
Discussion with the Owner regarding the dieting and the quality of life of the patient.

19/ Preparing the monthly Invoice to the Sponsor on the basis of the Fee List provided in the Protocol.

20/ Sending the monthly Invoice together with the Clinical Records, Assessment Forms from the owner and veterinarian, and any clinical and pathology Reports to Dr Mihaly Albert. (Payment of Invoices can only be made if accompanied by these data).

21/ Repetition of task under No 10 at the 6 month's conclusion of the clinical study.

22/ The return of unused CV 247 and wrappings to the Test Site chosen, together with the filled-in Return Forms provided in the Protocol.

RECOMMENDED HOME PREPARED DIET

With the drastic reduction of salt, sugar, fat, colouring, flavouring agents and preservatives, if possible from organic ingredients:

%	PROPORTION	PREPARATION	TYPE OF FOOD	CHOICES according to preferences of dog:
20	1/5	Raw	Fibrous vegetable	carrot, lettuce, apple, pear, banana etc
20	1/5	Cooked	Fibrous vegetable	cabbages, cauliflower, broccoli etc
20	1/5	Baked	Fibrous vegetable	oat flakes, muesli, brown bread
20	1/5	Cooked	Starchy, vegetable	potatoes, rice, pasta
10	1/10	Cooked	Animal	poultry, veal, rabbit
5	1/20	Slightly cooked	Animal	egg, boneless fish
5	1/20	Slightly cooked	Animal	liver (other than duck or goose)

Ready prepared commercial alternatives may be low calory food prepartions (e.g. those made by Eucanuba).

PATHOLOGICAL EXAMINATION

Any patient lost during the clinical study should be transported to an appropriate Institute for postmortem examination (such as the Pathology Department of Veterinary University) together with the PM Report Form provided in the Protocol with a request for its use for recording the findings, together with photographs and fixed tissue samples for histology of the relevant body areas. These are to be sent to the pathologist in charge of the CV 247 study (Dr Mihaly Albert)

If the postmortem examination at an appropriate Institute is not possible, it should be carried out by the veterinarian in charge of the case with records, photographs and tissue samples as above appropriately labelled for identification.

The loss of the patient should be notified on the last monthly Report.

IMPORTANT PROVISO

Should the Owner request the discontinuation of the study within the 6 month period, he should be asked for a last attendance at the clinic and the submission of the latest Assessment Forms.

The study records will be concluded with the signature of the owner and the last records will be sent in with the Invoice.

CONTACT DATA:

Director of Study: Dr Andor Sebestény
Mobile Phone: (in Hungary) 06-30-365-2857, (in Great Britain) 07951-704-082
E-mail: Andor.Sebesteny@cancer.org.uk

Dr Zita Kósa Test Site Manager
Mobile Phone: 06-30-463-5023
Surgery: 06-1-333-0948
E-mail: zitavet@beltav.hu

Dr Zsolt Sebestyén Test Site Manager:
Mobile Phone: 06-30-982-5735
Surgery: 06-1-394-1006
E-mail: sebestyen.zsolt@provet.hu

Dr Mihaly Albert Pathologist:
Mobile Phone: 06-20-910- 4989
E-mail: albert.mihaly@iif.hu
Address: 1191 Budapest, Artur-u 13. Fsz 1, Hungary

Invoice to be made out to: IVY Medical Chemicals PLC, 54 Sun Street, Waltham Abbey, ESSEX EN9 1EJ, UK

REFUND PROCEDURE FOR INITIAL PRE-ENTRY DIAGNOSTIC COSTS

When the Owner signs the Consent Form and CV 247 treatmant commences, the veterinarian in charge prepares an Invoice in the name of the Owner for the costs so far incurred.

The veterinarian will send in a copy of the initial pre-joining Invoice made out to the Owner after the first month of the study period, which will be honoured at the end of the study after the analysis of all data.

After 6 months, when all Assessement Forms from the Owner have been collected and submitted, all appointmens have been attended and the diet compliance was satisfactory, he will be entitled for these costs to be refunded.

SUGGESTED BLOOD TESTS

1. Full haematology

2. Reticulocyte % (in cases of 0.3 Ht or below)
3. Osmotic resistance
4. ALT
5. Alc. Phosphatase
6. TP
7. Albumin
8. Amilase
9. Lipase.
10. Glucose
11. Total Cholesterol
12. Triglycerides
13. Creatinine
14 Urea
15. Lactic Dehydrogenase
16. Creatine kinase (CK)
17 Total Calcium
18. Inorganic Phosphate