OCCASION

This publication has been made available to the public on the occasion of the 50th anniversary of the United Nations Industrial Development Organisation.

DISCLAIMER

FAIR USE POLICY

CONTACT

Please contact publications@unido.org for further information concerning UNIDO publications.

For more information about UNIDO, please visit us at www.unido.org

UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION
Vienna International Centre, P.O. Box 300, 1400 Vienna, Austria
Tel: (+43-1) 26026-0 · www.unido.org · unido@unido.org

RESTRICTED

18021

DP/ID/SER.A/1312
5 February 1990
ORIGINAL: ENGLISH

PESTICIDES FORMULATION AND APPLICATIONS

DP/POL/87/002

POLISH PEOPLE'S REPUBLIC

Technical report: Findings and recommendations*

Prepared for the Government of the Polish People's Republic
by the United Nations Industrial Development Organization,
acting as executing agency for the United Nations Development Programme

Based on the work of K.J. Brent, consultant
in bio-assay of pesticides

Backstopping officer: B. Sugavanam, Chemical Industries Branch

United Nations Industrial Development Organization
Vienna

* This document has not been edited.

V.90-81189

Contents

1. Summary

1.1 The author visited Poland for the period 28 November - 7 December, 1988 (2 days shorter than the original schedule, because of a family bereavement). The aim was to advise on the programme of evaluation of chemicals as potential pesticides at the Institute of Industrial Organic Chemistry (IPO) based mainly at Warsaw.

1.2 Visits were made to all relevant Departments of the Institute, including the branch at Pszczyna. Centres for collaboration in biological and toxicological testing at Skiernovicie and Lodz were also visited.

1.3 A lecture was given on 'The Search for New Crop Protection Treatments: Recent Trends' at IPO.

1.4 Suggestions regarding the enhancement of the range of crop protection targets, supply of chemicals, biological testing procedures and evaluation of results were made at a final discussion with the Director of IPO and senior colleagues.

2. Recommendations

The following points were suggested for consideration by the IPO management. It is realised that there are a number of constraints, particularly in finance, that could affect implementation.

2.1 Research objectives

The research concentrates on new mixtures and formulations, involving known active ingredients, for use in Polish agriculture. These do not require initial screening and can go directly to special tests, mainly in the field. With regard to truly novel chemicals, however, the Polish or even North European market would seem too small as an overall target area, bearing in mind the great costs of development these days. The initial biological testing should be adjusted to reveal world-wide potential, and later-stage testing should involve foreign collaborators.

2.2 Supply of chemicals

If screening for novel pesticides is to continue, it is important to increase the through-put of new chemicals. Ideally there should be

greater in-house synthetic chemical effort. Alternatively, funding of external collaborators should be increased to provide a greater volume of work, to provide costly intermediates, and to obtain candidate chemicals on an even year-round basis. The amounts synthesised could be reduced from ca. 5g to ca. 1 - 2g which should be sufficient for initial screening. Good active chemicals would then be re-synthesised for toxicological tests and third-stage screening. Chemicals made primarily as potential pharmaceuticals or dye-stuffs should be obtained and tested for pesticide activity.

On-line patent searching facilities should be arranged, preferably at IPO. All biological results should be submitted to chemists regularly throughout the year, and not on a year-end basis. These should be computerised to give easy storage and retrieval, and professional advice and costing should be obtained.

2.3 Biological testing

(a) Insecticides

The general approach is good, but there is a need for improved rearing facilities. Colorado beetle should be reared throughout the year. A Lepidopteran species should be included, and this will require increased glasshouse allocation. Considering world targets, Heliothis sp., leaf-hoppers and nematodes, and other major pests, should be considered for testing. Field screening facilties should be extended to warmer climates, e.g. Yugoslavia, to allow more regular infestations.

(b) Herbicides and PGRs

Important weed species should be used for primary screening, and crop plants introduced at the secondary stage. This system is now favoured by many companies. Tests could be re-designed to be done in one-half or less of the current space, using smaller plants, pots, spacing, etc. This would release glasshouse space for other purposes, and economise on the amount of chemical needed. Important world weed targets, e.g. Cyperus rotundus, should be considered as test organisms.

The question of PGR testing should be reviewed. Chances of success for PGRs with novel types of activity are considered small by many companies.

(c) Fungicides

Currently the testing is done mainly in vitro. Although cheap, such tests are of very limited value and should be used only as a back-up to in vivo tests where the chemicals are applied to small plants which are then inoculated with disease organisms. Suggestions for disease targets are made in the text. It is doubtful whether bactericide testing should be sustained; it appears very difficult to find broad-spectrum materials, and the agricultural importance of bacterial diseases is limited.

(d) General

There is an element of primary and secondary screening at Pszczyna. Whilst this is well done it would be more efficient to concentrate all the primary and secondary screening at Warsaw, and only a small expense would be required for this. At Pszczyna, field experiments would be the main screening activity, with some laboratory and glasshouse tests to extend information on active chemicals identified at Warsaw. Environmental testing, e.g. on bees, at Pszczyna is clearly valuable.

There appear to be around 50% university graduates amongst the screening staff; possibly over the longer-term there should be a higher proportion of assistant technicians, since much repetitive work is involved. Visits of screening managers and staff to foreign industrial organisations (e.g. in the UK and W. Germany) to study screening programme management and technology would be beneficial.

3. Introduction

A two-year UNDP-supported project (DP/POL/87/002) was initiated in 1987 in order to strengthen the long-term pesticide research programme of the Institute of Industrial Organic Chemistry (IPO) in Warsaw. This programme, which is funded primarily by the Polish government (Ministry of Industry), aims to increase the cost-efficiency and environmental safety of agricultural production in Poland, by enhancing the discovery and development of new pesticide molecules and formulations. Under the UNDP project, I had received two members of IPO staff, Dr. M.E. Turos-Biernacka and Miss M. Krawczyk, on UNIDO Fellowships at Long Ashton Research Station, Bristol, England, in May-July 1988, each for three months' training and experience in research methods.

The remit of the present assignment is given fully in UNIDO Job Description DP/POL/87/002/11-51/J13421. Briefly, it is to advise IPO on the biological targeting of chemicals as potential fungicides, herbicides and insecticides, including organisation, facilities, target organisms, test procedures and training needs. I arrived in Warsaw on 28 November 1988 and departed on 7 December 1988 - most unfortunately two days earlier than planned due to the death of my mother during my visit.

4. Research organised at Institute of Industrial Organic Chemistry

4.1 Remit and general approach

Much background information was provided before the visit in the UNIDO job description and in a letter received from the Director. Established in 1949, IPO is the only research centre in Poland responsible for the discovery of new pesticides and pesticide formulations. These are required in order to increase agricultural production, decrease environmental, user and consumer risks, and reduce expenditure on imported materials.

Roughly 1,500 new compounds per annum are now being screened for pesticide activity. Of these only 50-100 are produced in-house, the majority being obtained from at least ten other organisations in Poland - mainly University Departments of Chemistry - which collaborate with and receive financial support from IPO. Over the last 15 years ca. 10,000 new compounds were screened, and from these four new OP insecticides and one new plant growth regulator have been patented. Two of the insecticides, bromphenvinphos and methyl-bromphenvinphos were developed to the pilot-scale stage, for control of Colorado beetle on potato and ectoparasites of domesticated animals, and the former is fully registered for use in Poland. The growth regulator, a morpholine derivative (DMMC) related to mepiquat, is also registered and is now used commercially to a limited extent as 'Stimulen' specifically for the enhancement of stem elongation in flax.

Whilst novel chemicals are actively sought, the major emphasis is on the development of mixtures or new formulations of existing products which have advantages of efficacy, safety or economy in field use. The expertise of IPO in research leading to new synthetic and formulation processes is particularly strong.

4.2 Organisation

IPO employs about 800 staff - 550 at the central laboratories in Warsaw, 100 at the IPO biological research station at Pszczyna which I visited (ca 300 km SW of Warsaw), 100 at a pilot plant in Southern Poland, and the remainder at two smaller branches.

There are three Divisions - Pesticides (ca. 40% of total staff), Auxiliary and intermediate chemicals (ca. 40%) and Ecochemistry (safety, toxicology, analysis) (ca. 20%). Pesticides research and development is organised as follows:

IPO director
(Dr. W. Moszczynski)

Pilot Plant	Department of Analysis	Dept of Formulation	Department of Pesticide Application (Prof. E. Bakuniak)

Herbicides, PGRs Laboratory (Prof.J.Ostrowsky)	Insecticide and Acaricides Lab. (Prof.J.Kroczynski)	Fungicides Laboratory (Dr.J.Ptaszkowska)	Microbiology Laboratory (Dr.Cienecka)

Formal reviews of results, coupled with forward planning of third-stage tests, are made annually by a meeting in December of senior IPO staff from Warsaw and Pszczyna with industrial collaborators. Further discussions at a more detailed level are held with individual collaborating centres during December and January. Month-by-month project management is done through line management and through informal contact with collaborating departments.

4.3 Provision of experimental chemicals and formulations

Novel chemicals are produced mainly by external organisations as mentioned above. Production at each site varies considerably from year to year. The Technical Universities of Wroclaw (under Prof. Vitek) and Warsaw (under Prof. Amoski) are the leading producers, whilst other centres synthesise substantial numbers. IPO itself now synthesises only ca 50 new compounds per annum. Total throughput per annum has increased

steadily from 300, 15–20 years ago, to 1,400 in 1988; there is no clear maximum target, possibly twice as many could be screened without major changes in biological facilities. Emphasis is on exploitation of areas of chemistry known to have relevant pesticide activity. This demands a full knowledge of the patent situation in each area. This is achieved as far as possible by consulting Chemical Abstracts and other library sources; 'on-line' (computerised) searches of the patent literature are not yet available at IPO or in collaborating centres. I feel it would greatly increase efficiency and stimulate innovation in chemical synthesis to have such on-line facilities available.

Typically 5 g of each new chemical are first prepared for screening. Consideration should be given to reducing this target to 1 - 2g, since this could increase the numbers of chemicals produced, probably by 1.5 - 2-fold.

Chemicals are formulated for screening initially by dissolving in water on acetone, or as a wettable powder. This was said to be satisfactory, although in my experience insoluble chemicals are best dealt with by bead-milling in small containers with a dispersing agent to give suspension concentrates. Facilities for formulation for field testing are reasonably good, with special expertise in preparing emulsifiable concentrates. However, as in other laboratories, the equipment is ageing, and there is a specific lack of a viscometer.

Choice of chemical areas for synthesis seem to lie mainly with the external collaborators, according to their interests and experience. However, IPO staff keep abreast of world developments, through the literature and through attending major crop protection conferences such as the Brighton Conference, and new areas of chemistry can be considered as they arise. For some years, synthesis has focused on OP insecticides at Lodz, pyrethroid insecticides at the Polish Academy of Sciences, Warsaw, urea herbicides at Wroclaw, triazole fungicides at Szczecin and Warsaw Technical University, and phenylamide fungicides at the Silesian Technical University. The rationale for synthesising phenylamides should be reconsidered, in my opinion, in the light of the rapid development of resistance to this group by the potato blight fungus and other target pathogens.

Biological targeting of chemical synthesis or of the development of mixtures and new formulations is determined by the current main crop protection problems of Polish agriculture and horticulture, and contact

with research centres (I visited two of these at Skiernovicie) and the advisory services appear to be very good. The most urgent targets are as follows:

Group	Pest/pathogen/weed and crops
Invertebrate pests	Colorado beetle (Leptinotarsa decemlineata) on potato
	White butterfly (Pieris brassicae) on cabbage
	Spider mite (Panonychus ulmi) on orchard trees
	Onion fly (Hylemyia antiqua) on onion
	Rape beetle (Meligethes aeneus) on oilseed rape
	Green aphid (Myzus persicae) on sugar-beet
	White fly (Trialeurodes vaporariorum) on glass house crops
Vertebrate pests	Rodents and birds cause problems, but are not dealt with by IPO research
Fungi	Late blight (Phytophthora infestans) on potato
	Powdery mildew (Erysiphe graminis) on wheat and barley
	Glume blotch (Septoria nodorum and tritici) on wheat
	Bunt (Tilletia tritici) on wheat
	Scab (Venturia inaequalis) on apple
	Powdery mildew (Podosphaera leucotricha) on apple
	Leaf spot (Drepanopeziza ribes) on black-currant
	Powdery mildew on black-currant (Sphaerotheca mors-uvae)
	Downy mildews in vegetables and glasshouse crops (Pseudoperonospora cubensis)

Weeds	Silky grass (Apera spicaventi)
	Wild oat (Avena fatua)
	Couch grass (Agropyron repens)
	Goose foot (Chenopodium album)
	Chick weed (Stellaria media)
	Cleavers (Galium aparine)

Chlorfenvinphos and other OP insecticides, methoxychlor, Tedion, carbendazim, thiram, sulphur, copper oxychloride, 2,4-D, MCPA and TCA are manufactured in Poland. Other materials (including mancozeb, chlorothalonil, bupirimate, triadimefon, phenylamides, morpholines) are imported, mainly as active ingredients which are formulated in Poland. Each experimental chemical is submitted to IPO with a written statement of structure and physical properties and is given an IPO code number on arrival. It is submitted to all the biological screens. Results are fed back to chemists annually on sheets which cover all primary screening tests and secondary tests if available. Particularly good results are telephoned through immediately they are obtained - the minimum period is 2 - 3 months after arrival. Testing is often delayed for several months because the bulk of chemicals arrive in the autumn. Research centres tend to set their chemicals in annual groups, partly because analytical facilities are not available through the year. I believe that year-round steady submission of chemicals and return of results would aid structure-activity studies, speed up follow-up of activity, and enhance commitments from chemists, and should be sought actively. Computerisation of chemical acquisition and results is clearly warranted, aiming at an on-line network between IPO and collaborators. A professional appraisal of necessary software and hardware requirements and their anticipated costs should be made as soon as possible.

4.4 Bioassay of fungicides and bactericides

Primary and secondary screening is done mainly at IPO Warsaw. Approx. 8 people are involved in fungicide screening, against the following target fungi:

Alternaria alternata
Botrytis cinerea
Erysiphe graminis
Fusarium culmorum
Phytophthora cactorum
Rhizoctonia solani

Primary screening on approx. 30 chemicals per week, is done mainly in vitro, in slide germination (Alternaria and Botrytis) or agar plate (Fusarium, Phytophthora and Rhizoctonia) tests, chemicals being incorporated at rates between 10 and 200 ppm. Tests for Erysiphe are done on wheat seedlings, with protectant sprays initially at 500 and 1,000 ppm, in the greenhouse. In the primary screen only one or two rates are used, without standard chemicals. In the secondary screening standard chemicals are used, and a wider range of concentrations to give minimum inhibitory concentrations (MIC) for 100% control. Secondary tests also include application of seed infected with Fusarium, Helminthosporium and Aspergillus and dressed with experimental formulations to agar plates, to check for viability of the pathogens. Compounds active against Erysiphe are checked for systemic action by root application, and are also tested against Sphaerotheca fuliginea on cucumber and powdery mildew on Calendula (grown for pharmaceutical use).

Third-stage (field) screening is done mainly at IPO Pszczyna; however, primary screening on Phytophthora infestans is also done at Pszczyna on rye grains. Compounds active against Phytophthora infestans are evaluated in vitro on other Phytophthora species (cactorum, citricola, cinnamomi). Monitoring for phenylamide-resistant strains of P. infestans is also done at Pszczyna, with collaboration from Ciba-Geigy who provided controlled environment equipment. Other early-stage tests done at Pszczyna include those for activity against Fusarium culmorum in a rye grain test and Alternaria alternata and Venturia inaequalis in spore germination tests.

In anti-bacterial screening, 5 people are involved, for approx. 20% of their time (80% is on plant tissue culture aimed at pyrethrin production). Chemicals are tested initially at 20 ppm in agar plates against 5 bacteria:

Erwinia amylovora
Erwinia carotovora atroseptica
Pseudomonas lacrymans
Pseudomonas syringae
Corynebacterium michiganense

For the secondary screen several dilutions are tested to give an MIC value. If this is 5 ppm or less third-stage testing on plants is done at Pszczyna.

Third-stage tests are done on carrot and potato plants against E. carotovora, and on cucumber seeds against P. lacrymans. Testing is also done at Skiernovice for C. michiganense and E. amylovora in vivo.

Some 200 chemicals per year are tested, with 10 - 15 compounds going to third-stage tests.

I believe that considerable re-thinking is desirable on the pathogen screening programme. The use of in vitro tests makes a poor guide for activity in crop situations, and has been dropped as a main screening system by major agrochemical companies in general. It would be preferable to do primary screening for protectant action of sprays on seedlings, to give a good range of pathogen types, and to include major world targets. Such tests might include P. infestans on tomato, E. graminis on wheat, B. cinerea on lettuce, Pyricularia oryzae on rice, Cercospora sp. on peanut. More emphasis could be given to local targets, but costs of development are so large these days that it seems preferable to take a global view.

Whilst there is a shortage of effective anti-bacterial compounds, many companies are screening to some extent, without much success. Bearing in mind the relatively small markets for such materials, unless they are of very broad spectrum, I feel that anti-bacterial screening should be much reduced, and possibly terminated.

The splitting of primary screening between two sites is clearly unsatisfactory, and facilities for tests on P. infestans should be provided at Warsaw as soon as possible. Effort at Pszczyna could best focus on follow-up tests and field screening.

4.5 Bioassay of herbicides and PGRs

Chemicals are tested first against 10 crop species (3 monocots and 7 dicots), as pre- and post-emergence treatments, at 5 kg a.i./ha. Species are:

French bean
buck-wheat (Fagopyrum)
pea
mustard
cucumber
flax

rye-grass
maize
oat
wheat (may be replaced by a dicot in future)

These are placed in rows in mixed-species trays. Visual signs of herbicidal or PGR activity are recorded.

Active herbicidal compounds are submitted to secondary screening at 3 doses (typically 0.5, 1.0 and 2.0 kg/ha) on approx. 5 - 10 weed out of 15 - 20 available, selected according to the pattern of action in primary tests. Species include Stellaria media, Galium aparine, Avena fatua, Taraxacum officinale, based on the Polish weed flora. Tests are done mainly in small plastic pots.

Promising chemicals are submitted to further secondary tests at lower doses, and with separate pre- and/or post-emergence tests.

Secondary PGR screening is tailored to the type of activity seen in the primary screen, on relevant crop plants.

Consideration should be given to putting a selection of major weed species directly into the primary screen. Possibly 5 or 6 monocots and the same number of dicots, including major foreign weeds such as Cyperus rotundus and Echinochloa crus-galli. Crop species should be tested for selectivity at the secondary stage. These approaches are increasingly adopted by other organisations.

It should also be possible to reduce the space needed for testing, perhaps to 50%, by 'squeezing-up' the spacing of plants and reducing plant and container size. This would save light and glasshouse space, and also amount of chemical used.

The question of continuation of PGR testing at IPO needs careful consideration, particularly if weeds are to be used in future for primary herbicide screening. Chances of successful innovation are small; basically only growth suppressant and straw strengthening action appear to be found readily, and there are a number of materials available already. Some companies (e.g. ICI) have now dropped their PGR screening programmes. Novel PGRs obtained from other sources could always be examined directly by special third-stage tests.

4.6 Bioassay of insecticides and acaricides

Eight persons are involved. The primary screen is split into preliminary screen, used for all non-OP compounds, and a full screen used for OP compounds and for active compounds (ca. 100 per annum) detected in the preliminary screen.

Preliminary testing is done on two species, Musca domestica (25 µg/fly) and Tetranychus ulmi (0.1%).

Full testing is done on:

House-fly (M. domestica)) topical application
Oriental cockroach (Blatta orientalis)) at rates between 0.025
Colorado beetle (L. decemlineate)) and 20 µg/insect

Granary weevil (Sitophilus granarius)) dips or sprays at
Green pea aphid (Acertisiphon pisi)) 0.001, 0.01 and
Spider mite (T. ulmi)) 0.1%

If >90% kill at middle rates are obtained, secondary screening is done on the same target organisms, with more rates to give LD50 values.

Active chemicals are then selected for field-screening tests at Pszczyna and at Universities. Variation in insect populations with weather conditions can be a problem in these tests.

Insect-rearing facilities are at present limited, with inadequate temperature control.

These tests seem appropriate as far as they go, but a lepidopteran species should be incorporated, requiring increased glasshouse allocation. For world-wide markets such targets as Heliothis, leaf-hoppers and possibly a nematode should be considered. Failures in field-screening might best be avoided by arranging some field tests with collaborators in warmer regions, such as Jugoslavia, where insect infestations occur more regularly.

4.7 Field experimentation

Because of the time of year, I was unable to visit on-going field experiments. However, I was able to talk with some of the staff directly involved.

Early-stage field experimentation is done mainly at Pszczyna, although other centres (e.g. Skiernowicie) are also used as appropriate. At Pszczyna there are approximately 40 ha of land available, including 5 ha of orchard.

Micro-plot trials are done on a range of insect targets (Colorado beetle, cabbage caterpiller, cabbage fly, onion fly, rape beetle, spider mites, etc.); disease targets (potato blight, powdery mildew, eyespot, bunt, Septoria nodorum, Puccinia graminis on wheat, Rhynchosporium on barley, apple scab and mildew, black currant leaf spot, oak powdery mildew, etc.); weed targets (Apera spicaventi, Avena fatua, Agropyron repens, Chenopodium album, Galium aparine, Stellaria media, etc.). PGR field testing on a range of crops is also done; flax and linseed have received particular attention in recent years.

Typically 5-15 chemicals are tested per year, either novel chemicals from IPO screening or new mixtures and formulations. The field experimentation was said to work well overall, and the biggest difficulty seems to be obtaining regular infestations of the insect problems. It could be well worth arranging field screening of insecticides in warmer regions where infestations are more reliable, and where other insects of world-wide significance could be tested.

4.8 Toxicological and environmental evaluation

Toxicological studies are done at three centres, IPO Warsaw, IPO Pszczyna and Lodz. Initial toxicity tests, are done before the third stage (field) screening. Acute oral tests are done at Pszczyna, and any insecticide candidates with an acute oral LD50 below 50 mg/Kg, and fungicide/herbicide candidates below 150 mg/Kg are eliminated at this stage. Mutagenicity (by Ames test) is checked at Lodz, and mutagenic compounds are also eliminated at this stage.

A wider range of toxicity tests is done at various centres, including IPO Warsaw and IPO Pszczyna, and universities. IPO Warsaw appears to study mainly chemical intemediates whereas Pszczyna is concerned with potential agricultural products.

There is a clear case for centralisation of the toxicological effort, but of course considerable capital expenditure would be required.

Environmental studies are done mainly at Pszczyna. Here the dynamics of degradation in plants, soils and water are studied. Toxicity to bees, fish, plankton and earthworms is determined. Some field ecological observations are also made.

Documentation for registration is prepared mainly at IPO Warsaw, with input from all the collaborators involved.

I did not study in any detail the techniques for toxicological, environmental or residue testing since these will be the subject of a separate expert visit by Dr A. Calderbank.

5. Itinerary

Monday, 28 November: Arrived in Warsaw at 15.00. Taken to Forum Hotel.

Tuesday, 29 November: Formalities at bank and UNIDO. Met Dr. W. Moszczynzski, Director of IPO, and senior colleagues for overview. Visited Pilot Plant and Departments of Analysis and Formulation.

Wednesday, 30 November: Visited IPO branch at Pszczyna with Prof. Ostrowski, to discuss biological and environmental testing in the laboratory and field.

Thursday, 1 December: Visited Vegetable Research Institute (Prof. Dobrzanski and colleagues) and Institute of Pomology and Floriculture, at Skiernovici, to discuss collaborative biological testing.

Friday, 2 December: Visited Technical University (Dr. Bodalski), to discuss chemical synthesis and Academy of Medicine (Dr. Szalapinska) at Lodz, to discuss toxicological testing, particularly for mutagenicity.

Saturday/Sunday, 3/4 December: Sightseeing in Warsaw area; writing notes and preparing lecture.

Monday, 5 December: Visited Department of Pesticide Application, IPO, to study screening procedures.

Tuesday, 6 December: Met Prof. Ejmoski, Director of Pesticide Institute of the Technical University of Warsaw, at IPO, to discuss chemical synthesis. Gave lecture at IPO on 'The Search for New Crop Protection Treatments: Recent Trends'. Final discussion held with Dr. Moszczynski and colleagues, at which views and recommendations were outlined.

Wednesday, 7 December: Departed for London 08.00.

6. Acknowledgements

I am most grateful to all those persons in IPO and in the collaborating organisations who were concerned with my visit for their most helpful co-operation and kind hospitality. I am particularly indebted to Dr. Moszczynski for his overall interest and advice, to Professor Ostrowski for making such excellent arrangements for my programme and for accompanying me on visits, and to Mrs. Maria Turos-Biernacka for showing me such interesting places in Warsaw.