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Distr.
LIMITED
ID/WG. 282/98
17 October 1978
ENGLISH

C8561

UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION

INTERNATIONAL FORUM ON APPROPRIATE INDUSTRIAL TECHNOLOGY

New Delhi/Anand, India 20–30 November 1978

WORKING GROUP No.2

APPROPRIATE TECHNOLOGY FOR THE MANUFACTURE OF DRUGS AND PHARMACEUTICALS

APPROPRIATE TECHNOLOGY FOR THE PRODUCTION OF DRUGS AND PHARMACEUTICALS IN DEVELOPING COUNTRIES /

Discussion Paper

Appropriate Technology for the Production of Drugs and Pharmaceuticals in Developing Countries*

Issues and Considerations

Note prepared by the secretariat of UNIDO

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CONTENTS

Appropriate Technology for the Production of Drugs and Pharmaceuticals in Developing Countries*

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* This Note has been largely based on the background documentation on the subject, which is attached.

INTRODUCTION

1. World sales of drugs in developed market economies are concentrated in the hands of leading multinational firms. World-wide concentration of pharmaceutical production in 1970 and 1974 is given in Appendix I of this Note.

2. Appendix II of this Note shows the increasing share in the production of drugs by developing countries from 1960 to 1980. The share of developing countries in world production is estimated to go up from the present level of 12% to 14% by 1980. This increase in production will involve much higher capital investment than normally envisaged because, out of 110 developing countries, only about 10 have formulation and bulk production plants, while some 50 have only formulation plants and the rest only import the finished products. Therefore, a majority of them now only carry out the final stages of manufacture, e.g. formulating imported bulk drugs into finished preparations or repacking imported finished drugs. Backward integration of industries in these countries to go into more basic stages of manufacture will involve a considerable amount of capital investment without reflecting significantly on the value of output. The ancillary industries such as production of packaging materials and connected engineering industries for making simple equipment will also have to be established. These measures will result in a considerable increase in the value added and correspondingly reduce dependence on imports. With a simultaneous development of the chemical and chemical-based industries, where feasible, the developing countries will have a more self-sustained industry.

3. The trends from 1980 onwards are difficult to forecast because of the political, social, economic and technological factors that are likely to play an increasing role in the development of the pharmaceutical industry throughout the world. The growth of the industry will be more regulated to meet the urgent health needs of each country instead of the laissez-faire policy followed at present in many countries, especially as the right to health care will get widely established as a major socio-political goal. This will also mean higher levels of government economic controls both on prices

and profits and foreign capital investment. To avoid the present concentration of drug distribution in urban centres, and overcome the lack of availability of drugs in rural and remoter parts of developing countries, the trend will be towards public acquisition of the drug distribution systems. In developing countries, more and more semi-industrial units such as formulation plants, hospital pharmacies and multi-purpose production units will be set up and dispersed all over the country to meet the requirements of the population who at present get little or no benefit from modern medicine. These will supplement the existing larger units operating in urban centres in the more advanced developing countries. Traditional medicine will also play a more important role in the health services and greater attention will be paid by governments to the standardisation and upgrading of products from this source.

I. OBJECTIVES

4. The major objectives in promoting the pharmaceutical industry are:

(a) To provide, in adequate quantities, products essential to the health care of the population at prices that are within the reach of the majority of the population.

(b) To set up a relatively independent drug industry which gives developing countries more freedom to form health care policies that are relevant to their particular needs at minimal cost, using locally available raw materials and production facilities and also utilising the existing traditional forms of medicine.

(c) To contribute to the national economy of the developing countries.

By taking steps depending on the stage of development of the industry in these countries: starting from formulation of drugs to dosage forms, operation of multi-purpose plants, producing bulk drugs of plant and animal origin, producing drugs from intermediates, the establishment of a self-sustained industry can be progressively achieved, which can be designed for a variety of end-products, thus giving the industry a commercial and economic advantage over other forms of modern industry. The technology for establishing such production is fairly well diffused and can be obtained relatively easily from small developed countries or advanced developing countries in a form adapted to the needs of developing countries.

The development of the pharmaceutical industry usually spearheads the development of chemical and chemical-based industries, as well as the ancillary products and engineering industries required to cater to their needs and has, therefore, a catalytic effect on industrial development in general.

(d) To provide opportunities for yound men and women to learn new disciplines of science and provide employment for trained people. In countries where drug and associate industries are established, opportunities are provided for young people to keep pace with the rapid strides of scientific development around the globe, and in the aggregate consitute the spearhead of a technological society.

II. CONSIDERATION OF TECHNOLOGICAL ALTERNATIVES

5. The choice and adaptation of appropriate technology in promoting the pharmaceutical industry in different groups of developing countries have been discussed in the background paper.[1/] Even in developing countries which are fairly advanced, where products are made in economic-sized units and located where the necessary infrastructure like chemical and engineering industries exist, it is possible for semi-industrial units dispersed over the rural and remoter parts of the country also to be set up to formulate basic drugs relevant to the region, to meet the local needs and also to draw their requirements of raw materials from multi-purpose plants located nearby. The size of these semi-industrial units, their capital cost and the testing facilities required to maintain quality are also indicated in the background paper.[2/]

6. These units will supplement the major production plants and cater to the needs of the population of rural areas who are receiving hardly any of the benefits of modern medicine today.

7. The size of the formulation unit suggested in the background paper,[3/] Appendix I, is based on what the average control laboratory can cater to. If, however, it becomes necessary to set up smaller-sized units, depending on demands, it will become necessary to link

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1/ Choice and Adaptation of Appropriate Technology in Production of Drugs and Pharmaceuticals - ID/WG.282/93.

2/ Ibid.

3/ Ibid.

two or more formulation units to one control laboratory, provided the distances over which the samples have to be moved are not too great. The use of raw materials and marketing of finished products in such cases will, however, have to await clearance of samples of each batch by the control laboratory.

8. It is necessary to ensure that the products turned out by these units have the required bio-availability (see Appendix IV of the background paper[1]) and, for this purpose, assistance from other well-established units or institutions within the country is necessary. A small product development laboratory (research laboratory, attached to the control laboratory) to work out any problems that may be encountered is also suggested in Appendix IV, and Appendix I of the background paper.[2]

9. While formulation facilities can be economical in small markets, and assist in developing skills to undertake backward integration into basic manufacture, economies of scale become very important in the production of antibiotics, drug intermediates and synthetic drugs. Many developing countries have already developed technological capability and adapted improved technology to their specific needs and environments. Some have by their local R and D efforts improved on the productivity of imported processes. But in such cases there is also a well-developed chemical industry, including a petrochemical industry, to supply the basic chemicals and integrate development of chemical-based industries such as dyes, plastics, synthetic fibres, pesticides, rubber chemicals, surfactants, etc., which makes the production of common chemical intermediates feasible, thereby linking the gaps between the chemical industry and intermediates for drugs, dyes, etc.

10. In developing countries, a large portion of the population depends on the indigenous systems of medicine. To improve their usefulness the systems need to be standardized and upgraded after a proper screening programme. In addition to improving the reliability of the products, it will be necessary to weed out many useless preparations that have come into existence and have been responsible for

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1/ Choice and Adaptation of Appropriate Technology in Production of Drugs and Pharmaceuticals - ID/WG.282/3.

2/ Ibid.

exploiting the public. The methods to be adopted by different countries will not be the same, but some indication to developing countries as to how best they can improve these systems of medicine and make them more effective are suggested in the background paper.1/

III. POLICY IMPLICATIONS OF ALTERNATIVE TECHNIQUES

11. The following is a listing of main issues:

(a) Establishment of a national list of drugs as a basis for rational development of the pharmaceutical industry in relation to the needs of the public health care industry.2/

(b) Improvement and strengthening of the scientific bas for development and production of the traditional medicine and household remedies.3/

(c) Development of repacking and formulation plants.4/

(d) Development of manufacturing plants for sanitation-related products, in particular water treatment agents, pesticides, and disinfectants.5/

(e) Formation of an intra-sectoral framework to advance the development and production of bulk drugs, including immunologicals and antibiotics as well as their related basic materials such as intermediates, biologicals, plant products, chemical precursors and various nutrient media.6/

(f) Study and establishment of standards for tropical conditions, chemical engineering plant facilities and layout structures. Dosage forms also should be designed to withstand high temperature and humidity conditions in tropical countries.

(g) Development of manufacturing plants for dosage packaging (e.g. pharmaceutical glass) and various other types of packaging materials.7/

1/ Choice and Adaptation of Appropriate Technology in Production of Drugs and Pharmaceuticals - ID/WG.282/93.

2/ Report of the Second Panel Meeting of Industrial Experts on the Pharmaceutical Industry, Annex I, p. 21 - ID/WG.267/4/Rev.1*

3/ Choice and Adaptation of Appropriate Technology in Production of Drugs and Pharmaceuticals - ID/WG.282/93. and Medicine for the Rural Population in India, Chapter I - ID/WG.282/68.

4/ Ibid.

5/ ID/WG.282/93.

6/ ID/WG.282/93.

7/ Appendix I - ID/WG.282/93.

* to be distributed at the meeting.

(h) Establishment of a comprehensive quality assurance system including the specification of standards and procedures, training of specialized personnel, information training to all persons concerned, in-plant QA systems, inspection and auditing and verification methods relating to the total materials and products stream including the storage, administering and usage of drugs.1/ A system of registration of drugs taking into account the usefulness of the drug to the health of the population vis-à-vis risks of toxic effects due to overdosage and other factors should be established. This could be done on a regional basis for smaller countries which cannot afford the elaborate facilities needed.

(i) Establishment of regulations relating to domestic and foreign corporate ventures, the importation of foreign drugs, intermediates and/or technological know-how.2/

(j) Establishment of model manufacturing units in less developed countries and in the rural areas of more advanced developing countries. These units will formulate:

(i) Selected drugs of the indigenous systems of medicine;

(ii) Household remedies;

(iii) Antiseptics;

(iv) Infusions for rehydration; and

(v) Other simple formulations depending on the common ailments of the area.

A schematic layout plan of such an unit is given in one background paper.3/ The socio-economic benefits that will be derived from the proposed programme are also illustrated.4/

(k) Establishment of multi-purpose plants to produce drugs from intermediates for a group of model manufacturing units.5/

(l) Establishment of units for extraction of active ingredients of plant products that can be cultivated in developing countries instead of the present practice of exporting them as crude drugs to developed countries. This will improve the value added of the products exported to developed countries and give the developing countries the necessary foreign exchange reserves to import intermediates, etc. required for the manufacture of drugs to combat diseases common in the area.

1/ Medicine for the Rural Population in India - ID/WG.282/68.

2/ Report of the Second Panel Meeting of Industrial Experts on the Pharmaceutical Industry - ID/WG.267/4/Rev.1.*

3/ Medicine for the Rural Population in India - ID/WG.282/68.

4/ Ibid.

5/ Choice and Adaptation of Appropriate Technology in Production of Drugs and Pharmaceuticals - ID/WG.282/93.

12. The above issues also reflect the main elements of alternative technological development strategies for establishing a pharmaceutical industry, taking into account the development requirements of a particular country.

IV. THE ROLE OF INTERNATIONAL CO-OPERATION

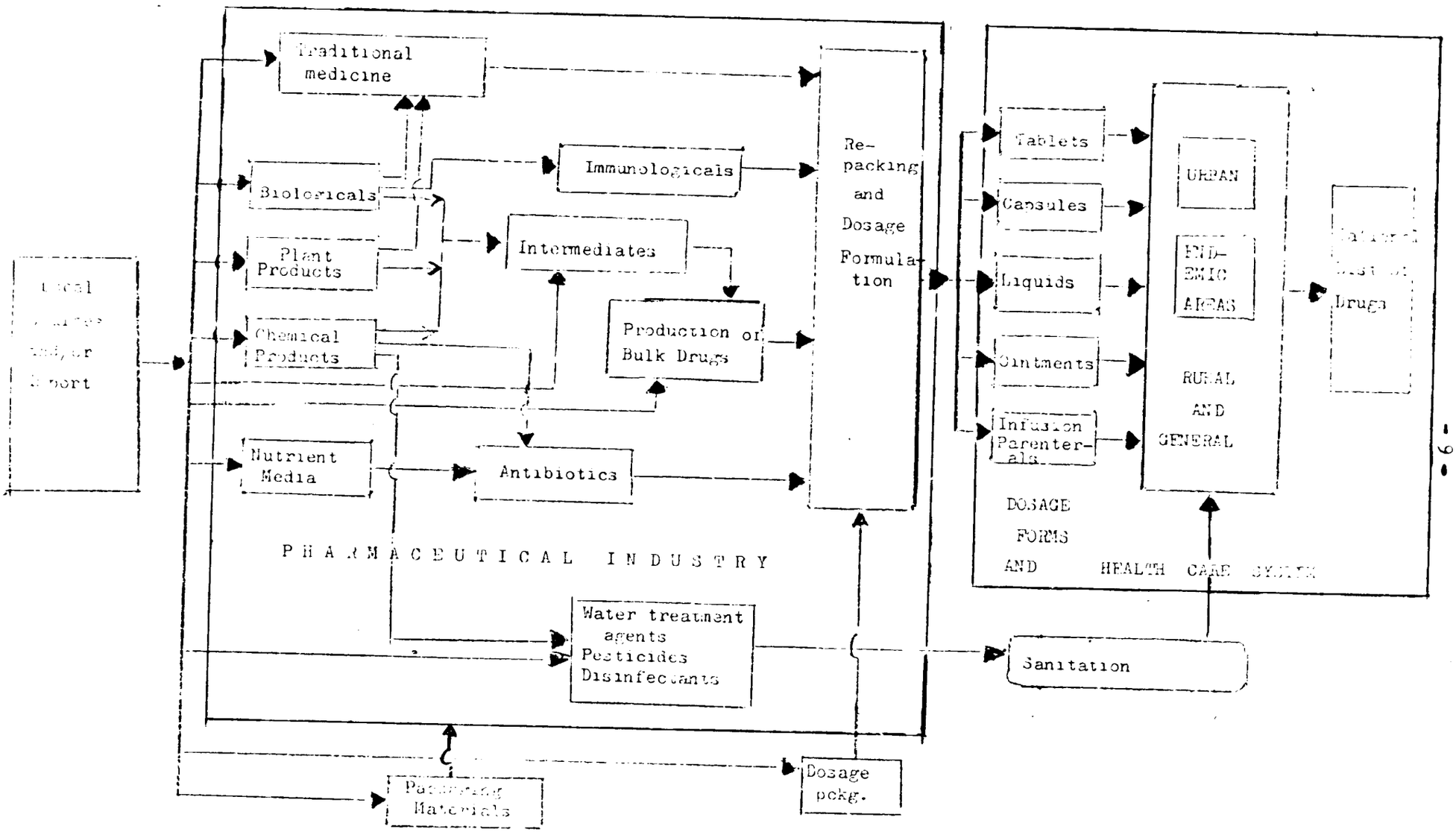
13. In the pharmaceutical industry there is a high rate of obsolescence of products, not only due to the discovery of improved products or cheaper substitutes, but because the users over a period of time are known to become sensitized to certain drugs or, what is equally important, the micro-organisms against which the drug action is directed, after its wide use, develop a resistance. In both cases, the drug loses its efficacy and becomes obsolete due to this natural phenomenon. Under the circumstances, efforts to update the technology used and products manufactured by the larger units and Government research institutions — who can afford the expenditure involved on R and D — are essential. Large manufacturing units in developed countries which have established modern research laboratories and spend a considerable portion of their sales turnover on R and D are the main source of information even to the more advanced developing countries today, as regards both improved processes and strains and newer drugs, and will hold a commanding position in this regard for quite some time. Association with such units and maintenance of flow of information is therefore essential.

14. In less developed countries both special experience in management methods and technical expertise in running pharmaceutical units are lacking. Manufacturing operations have to be carried out under hygenic and often sterile conditions, with scrupulous attention to quality and personnel need to be trained in working in such an environment. The developing countries should therefore, seek assistance in this regard from international companies. Training facilities for managerial personnel and technical staff at the factory level are therefore essential and international co-operation in this regard will be most useful to developing countries.

15. For dissemination of scientific information to the medical profession on the action of newly-introduced drugs, toxic effects, treatment of toxic effects and precautions necessary, based on experiences

encountered during clinical trials and those reported from time to time, the developing countries essentially depend on their foreign collaborators. A flow of information in this respect from the international firms concerned is very essential.

16. International collaboration therefore still plays an important role in this industry and for developing countries to obtain greater benefits from such collaboration, certain guidance is necessary. Governments can also establish certain guidelines in regulating collaboration arrangements to obtain the maximum benefits in this regard.



FLOW CHART PHARMACEUTICAL INDUSTRY AND HEALTH CARE

Appendix 1

World-wide Concentration of Pharmaceutical Production

1970 and 1974

Sales	1970		1974	
	Millions of Dollars	Percentage	Millions of Dollars	Percentage
Total sales of developed market economies	18,633	100	34,001	100
Sales of leading 10 firms	4,987	27	9,498	28
Sales of leading 20 firms	7,748	42	14,561	43
Sales of leading 30 firms	9,249	50	17,682	52

Ref: UNIDO publication ID/204, Sales No. E. 78.11.34

Appendix II

Year	1960	1975	1980
Developing Countries of Africa, Latin-America and Asia	8.40[1])	12.00[3])	14.00[5])
Industrialized Market Economy and Centrally Planned Economy Countries	91.60	88.00	86.00
Total	100.00[2])	100.00[4])	100.00

Unit : percentages

Source of basic data : **Summary of the Draft, World-wide Study of the Pharmaceutical Industry, UNIDO/ICIS.76.** (47 pp.)

Notes : (1) Estimated distribution : Africa (0.18 %), Latin-America (4.80 %) and Asia (3.42 %).
(2) 1960 value of world production US $ 7.9 billion
(3) Estimated distribution : Africa (1.29 %), Latin-America (6.30 %) and Asia (4.41 %).
(4) 1975-value of world production US $ 37.5 billion
(5) Indicative only; estimates extrapolated on the basis of share-increases during the period 1960-1975 would lead to share percentages, ranging from 13.2 to 14.5 %.

WORLD PRODUCTION OF PHARMACEUTICALS

(share of developing countries)

In preparing this Note, material contained in the following background papers has also been used:

1. Provision of Drugs by Appropriate Technology - ID/WG.282/45.
2. Medicine for the Rural Population in India - ID/WG.282/68.
3. Choice and Adaptation of Appropriate Technology in Promoting Healthcare in Zambia - ID/WG.282/69.
4. Appropriate Technology in Drug and Pharmaceutical Industries - ID/WG.282/79.
5. Aspects of Developing the Pharmaceutical Industry in Brazil - ID/WG.282/72.
6. Arab Company for Drug Industries and Medical Appliances - ID/WG.282/77.
7. A Case Study of the Pharmaceutical Industry of the Republic of Korea - ID/WG.282/94.
8. Choice and Adaptation of Appropriate Technology in Production of Drugs and Pharmaceuticals - ID/WG.282/93.

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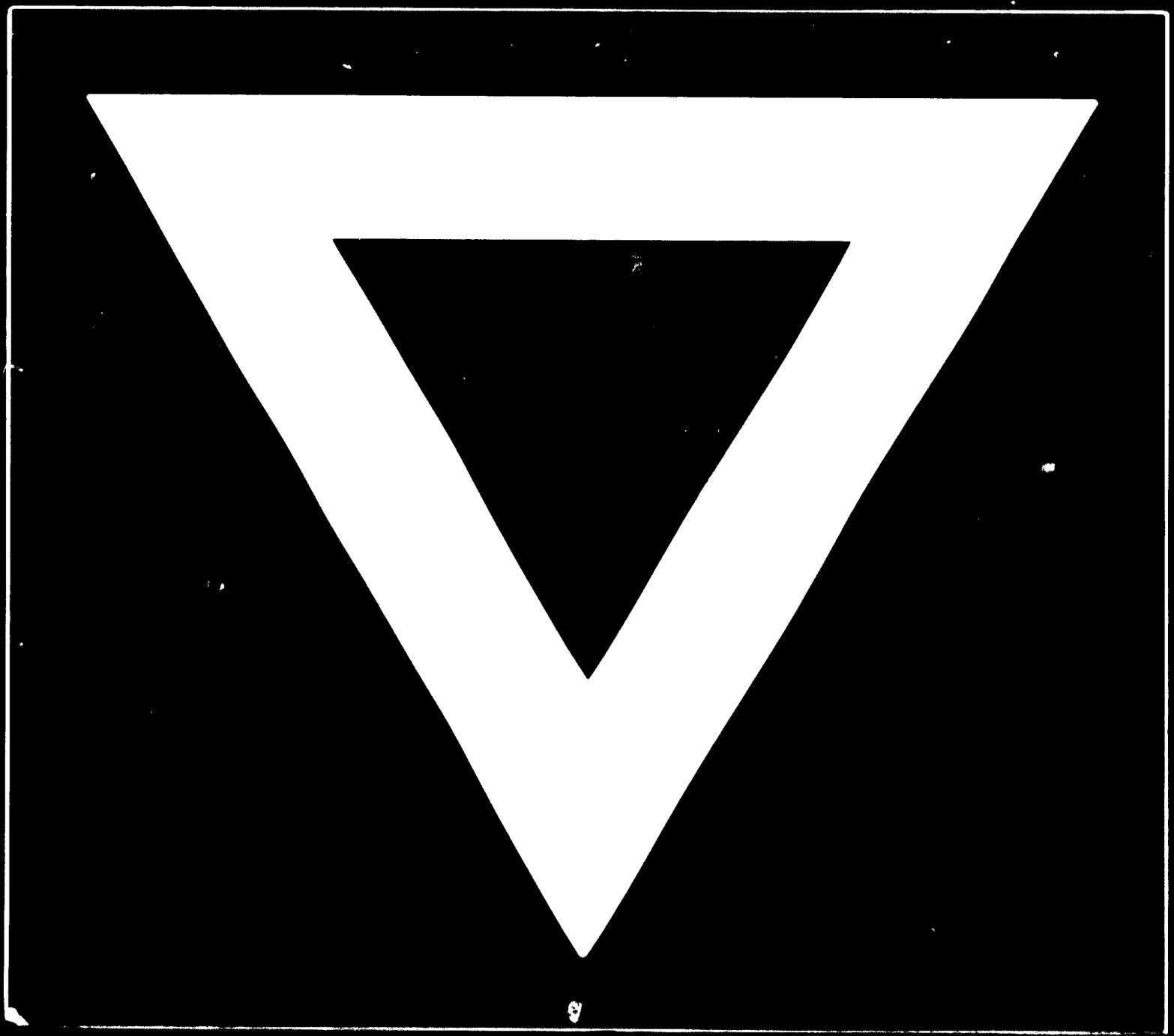

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