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# PRODUCTION OF STANDARDS AND REAGENTS FOR THE QUALITY CONTROL OF MEDICINES

DP/VIE/84/006

SOCIALIST REPUBLIC OF VIET NAM

Technical report: Production of Chromatographic Adsorbents*

Prepared for the Government of the Socialist Republic of Viet Nam
by the United Nations Industrial Development Organization
acting as executing agency for the United Nations Development Programme

Based on the work of R. Toman, expert in the production
Chromatographic Adsorbents

Backstopping Officer: Ms. M. Quintero, Chemical Industries Branch

United Nations Industrial Development Organization
Vienna

* This document has not been edited.

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## ABSTRACT

Production of Chromatographic Adsorbents

DP / VIE / 84 / 006 / 11-02

Purpose of the project is strengthening of the Standards and Reagents Section of the Institute of Drug Quality Control , Hanoi , Vietnam in production of various grades of silica gel for column,thin and thick layer chromatographies,GC and HPLC,and of microcrystalline cellulose both in improved quality and increased quantity.The duration of the activity is scheduled for two 3 weeks split missions.

The production of various grades silica gel has been demonstrated at both laboratory bench and pilot plant levels as per availability of apparatus, chemicals and raw materials.The main objective to upscale the production of silica gel has been achieved.

Four different types of silica gels for thin layer chromatography were prepared and tested.

An original method using potassium hydrogen sulphate has been demonstrated to enlarge pore size of silica gels.

Methods for standardization and specification of the silica gels produced have been introduced.

The consultant recommended a careful monitoring of ion exchange technology of silica gel production,preparation of high purity binders for TLC chromatography and analysis of batch samples according to given criteria.

## CONTENTS

## INTRODUCTION

The Government of Vietnam,in accordance with the Five Years Development Plan,attaches a great importance to the local production of different types and grades of adsorbents for allowing relative self-sufficiency and savings scarce,foreign currency.To achieve this goal, it is necessary to provide basic tools for production and testing of these adsorbents and to provide basic standards and reagents.

The Institute of Drug Quality Control (IDQC) has been established in Hanoi in 1971,with a subunit in Ho Chi Minh City.The main functions of the Institute are :

- To control the quality of medicines,their intermediates raw materials with regard to their production.
- To study various methods of testing and standardizing the quality of drugs.
- To produce various adsorbents,reference substances and analytical biochemical reagents.
- To disseminate scientific and technical information.

UNDP/UNIDO is supervising a project the purpose of which is the strengthening of the standards and reagents section of IDQC,to increase its services to the pharmaceutical industry,to provide standards, reference substances,reagents and adsorbents both in improved quality and increased quantity to provincial drug quality control institutes, pharmaceutical factories and other public health related institutions.

UNDP/UNIDO by way of inputs for this project is strengthening the infrastructure facilities of the adsorbent production section for achieving its proposed outputs as follows :

- Production of various grades of silica gel for chromatography (column,thin and thick layer,GC,HPLC)
- Production of silica gel for TLC with fluorescent indicators.
- Production of pre-coated silica gel plates or sheets.

- Production of large pore size silica gel for both GC and HPLC
- Preparation of spherical particles of silica gel for GPC, GC and HPLC
- Preparation of inert silica gel for the use in GC and HPLC
- Production of microcrystalline cellulose and its derivatives.

This part of the project when fully implemented should result in both an increased production of silica gels and production of new materials on its basis. The aims proposed will facilitate efficient and wide coverage of quality assurance programmes of many essential drugs in the country.

## TERMS OF REFERENCE OF THE CONSULTANT

Duties and activities of the consultant (expert) in the production of chromatographic adsorbents as indicated in the job description are :

- Train counterpart staff in the production, quality improvement and testing of adsorbents including TLC material with fluorescent indicators.

- Advise on processes and methods for the production of silica gel of large pore size for the use in GPC, GLC, HPLC.

- Advise on improvements and technologies for the production of microcrystalline cellulose and its derivatives.

- Recommend processes and methods for increased production of adsorbents and introduction of additional ones.

## WORK ASSIGNED TO THE CONSULTANT

The consultant arrived at Hanoi on 22nd April 1990 and was received by CTA of the project. The consultant reported to work at the Institute of Drug Quality Control on 23rd April 1990 and was briefed shortly by the CTA about the present status of the project, main goals and facilities available for his work.

On the same day,the consultant was officially welcomed by the staff members of the Institute including the National project Director.The modelalities regarding the implementation of various terms of reference of the consultant were discussed.Later on,the consultant was conducted by the NPD round the various departments of the Institute.

## ACTIVITIES OF THE CONSULTANT

The consultant started immediately with his activities which were assigned to him according to the job description.However,most of its activity was restricted to bench level due to insufficient quantity of some basic raw materials,chemicals and also due to non-availability of critical apparatus,which had been ordered a long time ago but were lost either in mail or have not arrived yet.However,despite of these severe constrains.the consultant made the maximum efforts to demonstrate both methodology and techniques which should enable production of various types of silica gels used in chromatographic methods .Much more could have been done with the availability of all necessary chemicals and apparatus.

### A. PRODUCTION OF SILICA GEL

In the past, silica gel was prepared by the reaction of water glass with acids.Using this method a solution of water glass was mixed with aqueous solutions of sulphuric or hydrochloric acids.Rarely,other acids, e.g.acetic acid,phosphoric acid,formic acid,and nitric acid were used,too. The main factors influencing the quality of the product desired were besides the $SiO_2$ concentration and temperature,the final acidity of sol which influenced considerably the physico-chemical properties of the product (pore size,pore volume,specific surface area,etc. ).Thus pH values had to be regulated according to the needs for each type of silica gel. Hydrosol of silicic acid coagulated to hydrogel followed by syneresis and a diluted solution of $Na_2SO_4$ was excluded.The intermediate product was washed with a large quantities of water in order to separate $Na_2SO_4$ from the gels.Various chemicals were added to elution water in order to influence secondary pore size.The washed gel was dried,activated,

sieved and packed according to parameters required.

The most recent production of silica gel applies removal of sodium from the water glass by the use of ion exchangers. Advantage of this procedure is in obtaining a very pure homogeneous product with a predetermined pore size, which can be achieved by an easy pH control of a sol. Low content of salts enables to omit a very laborious and time-consuming washing of the gel, which is necessary in the case of mixing method of silica gel preparation by the use of acids and silicates soluble in water. The cation exchanger is regenerated easily by elution with 5% aqueous solution of hydrochloric acid. Ion exchange technology has found a widespread application all over the world and the main procedures of silica gel in the Eastern and Western countries are using this approach.

In the Institute of Drug Quality Control, Hanoi, Vietnam they have also developed a bench scale production of silica gel. The procedure is as follows:

Water glass (2.5L) with $SiO_2$ content 28.5%, density 1.386 is diluted with water (12L) and aqueous ammonium hydroxide (0.5L). The solution is deionized on a Wofatit KPS 200 column (12X94 cm) with an elution rate 0.75L/min. Elution of silicic acid is monitored by pH measurement. When pH of the eluate reaches ~ 6 elution of the column is terminated. Usually, 15 L of silicic acid sol is collected with pH ~ 3. Aqueous solutions of 1M sodium hydroxide (135ml) and 10% ammonium hydrogen carbonate (375 ml) are added to bring pH of the sol to neutral. The gel is aged for 24-36 h and then dried at 110° for 2-3 days. The silica gel prepared is milled, decanted and sieved. Using this procedure three types of silica gel were prepared:

| | |
|---|---|
| Silica gel S.K | Particle size 5-40 µm |
| Silica gel S.K | Particle size 40-100 µm |
| Silica gel S.K | Particle size 100-160 µm |

However, the most important charateristics, i.e specific surface area, specific pore volume, and average pore radius were not determined.

Because of the lack of apparatus, which would enable estimation of these important criteria, the expert proposed very simple methods for this purpose.

## DETERMINATION OF SPECIFIC SURFACE AREA

Approximate data useful at least for comparison of various silica gels in routine tests, are based on titrations of a silica gel suspension, using dilute sodium hydroxide solution, from pH 4 to 9 at 25°C. There was established a linear relation between specific surface area (BET) of many silica gels and, the consumption of 0.1M sodium hydroxide solution.

## PROCEDURE

A sample of silica gel, e.g. 1.5g is dried at 300°C for 2 h. Sodium chloride (30g) is added to the weighed silica gel sample and the volume is made up to 150 ml with distilled water. The pH of the suspension is brought to 4 with dilute hydrochloric acid. 0.1M Sodium hydroxide solution is added slowly from the burette, stirring continously, until pH 9 is reached. After each addition the attainment of a sensibility constant pH is awaited. The specific surface area $m^2/g$ is calculated with the help of the empirical equation :

Specific surface area $O = 32 \times V - 25$ $(m^2/g)$

V=consumption of 0.1M sodium hydroxide from pH 4 to 9, in ml.

The following results were obtained:

| | Specific surface area ($m^2/g$) |
|---|---|
| Silica gel S.K. (5-40 µm) | 386 |
| Silica gel S.K. (40-100µm) | 455 |
| Silica gel S.K. (100-160µm) | 485 |

The values are reproducible for different samples of one and the same silica gel. A special advantage of the method is that it can be applied also to plastic polysilicic acid gels, i.e pre-cursors of silica gel. The values for the specific surface area of a plastic polysilicic acid gel and for the corresponding xerogel can be closely similar.

There is so far no final answer to the question how far agreement exists between the surface area values for silica gel obtained by the BET-method and by the titration method. The letter is nevertheless frequently used.

## DETERMINATION OF THE SPECIFIC PORE VOLUME

A simple method for approximate determination of the specific pore volume has been described.It is based on the observation that whereas dried,fine-grained silica gel is a mobile powder,the grains adhere to each other and cake when the pores have been filled with water.

## PROCEDURE

A sample of silica gel is dried at 300°C for 2 h.1 g of dried silica gel is titrated with water at one drop per minute,stirring continuously.After each addition,the mixture is left until the liquid is uniformly distributed and the silica gel powder appears dry again.The approach of the endpoint is heralded by parts of the silica gel powder adhering to the vessel wall.The end point is a visible caking together of the powder.The titration in ml per gram silica gel sample corresponds to the ml pore volume per gram substance.The technique requires practice but is suitable for rapid comparision of silica gel preparations

The following results were obtained :

| | Specific pore volume ($cm^3/g$) |
|---|---|
| Silica gel S.K.(5-40$\mu m$) | 0.37 |
| Silica gel S.K.(40-100$\mu m$) | 0.73 |
| Silica gel S.K.(100-160$\mu m$/) | 0.79 |

## DETERMINATION OF AVERAGE PORE RADIUS

The average pore radius can be calculated approximately by picturing the total mumber of pores as a single cylindrical pore from the figure.

$$\text{Average pore radius } r = \frac{2 \times \text{specific pore volume } V}{\text{specific surface area } O}$$

The following results were obtained :

| | Average pore radius ( $nm$ ) |
|---|---|
| Silica gel S.K.(5-40 $\mu m$ ) | 2 |
| Silica gel S.K. (40-100 $\mu m$ ) | 3.2 |
| Silica gel S.K. (100-160$\mu m$ ) | 3.25 |

## PRODUCTION OF SILICA GEL AT A PILOT PLANT LEVEL

The expert made calculations of the amounts of Wofatit KPS 200 ion exchanger and water glass needed for an upscaled production of silica gel. With certain limitations and absence of the proper equipment for balancing optimal conditions, he proposed the following procedure for a pilot plant production of silica gel.

### PROCEDURE

7.9 L of water glass (23.5% $SiO_2$, 10.07% $Na_2O$, d=1.386) is diluted with 44 L of water and 2 L of ammonium hydroxide to achieve ~ 5.5% $SiO_2$ concentration. The solution is deionized continuously on a column (20 x 110 cm) of Wofatit KPS 200 ion exchanger (ion exchange capacity 2 mekv /ml) at a flow rate ~ 1 L/min. Elution of silicic acid is monitored by pH measurements. When pH reaches the value of washing water, elution of the column is terminated. 58L of silic acid sol is collected. pH of the solution is brought to 6.3 by addition of 1M NaOH(464 ml) and 10% $NH_4HCO_3$ (1450 ml). The gel is aged for 36-48 h, dried at 120°C for 2-3 days. The silica gel prepared is milled, decanted and sieved.

Because of shortage of time, the expert does not consider all the parameters given to be optimal and they should be found after the consultations with the expert by the staff members in a near future.

This concerns mainly the optimum amount of water glass applied onto the ion exchanger column, flow rate, monitoring of the silic acid in the eluate, determination of the $SiO_2$ and $Na_2O$ contents in silicic acid sol, adjustment of proper pH for gel formation, etc. Nevertheless, using the above mentioned procedure, provided that all three ion exchange columns are in operation, a daily production of silica gel is increased more than 9 times.

Regeneration of ion exchange columns is accomplished by 5% aqueous solution of hydrochloric acid. All these operation can be done within a one day cycle.

## PRODUCTION OF SILICA GEL FOR THIN LAYER CHROMATOGRAPHY

For thin layer chromatography (TLC), silica gel with the particle size 5-40 μm is frequently used. However, better separations are achieved with

narrower particle size distribution.

Four basic types of silica gels for TLC could be produced at the Institute of Drug Quality Control in Hanoi:

Silica gel S.K. (5-40 μm) without additives

Silica gel S.K.$L_{254}$ (5-40 μm) with fluorescent indicator

Silica gel S.K.G (5-40 μm) with 13% of gypsum

Silica gel S.K.G.$L_{254}$ (5-40μm) with 13% of gysum and with fluorescent indicator

Silica gel S.K.G is prepared by mixing dry silica gel (5-40μm) with 13% (w/w) of pure gypsum.

Silica gel S.K.$L_{254}$ is prepared by mixing dry silica gel (5-40μm) with 0.2-0.5% (w/w) of fluorescent indicator (Fluoreszenz-indicator $F_{254}$,Merck,Darmstadt,W.Germany).

Silica gel S.K.G.$L_{254}$ is prepared by mixing dry silica gel (5-40μm) with 13% (w/w) of gypsum and 0.2-0.5 % (w/w) of fluorescent indicator (Fluoreszenz-indicator $F_{254}$,Merck,Darmstadt,W.Germany)

Fluorescent indicators are of inorganic and organic origin.

Frequently used inorganic indicators are :zinc silicate,zinc cadmium sulphide,calcium halophosphate N83 White,etc.

Organic fluorescent indicators : various pyrene derivatives; sodium salts of 3-hydroxypyrene-5,8,10-trisulphonic acid,3,5 dihydroxy-pyrene -8,10-disulphonic acid,cyanine dyes (UV 366.Mixing with organic fluorescent indicators is often impracticable.These substances are soluble in solvents of polarity appropriate for development and elution.

## PREPARATION OF TLC PLATES WITH STARCH AS THE BINDER

Silica gel S.K or silica gel S.K.$L_{254}$ are mixed with water to get a mixture of the proper consistency .Starch is added in the weight of 3-4% on the weight of dry silica gel.The slurry is heated on a water bath with vigorous stirring.At 80°C,starch present in the slurry changes its viscosity properties.Slurry is becoming more viscous.Mixing is continued

for ~30 min. After cooling, the viscosity of slurry should be suitable for coating TLC plates. Plates are dried at room temperature or at 105°C for 15 min.

An alternative method is as follows.

Materials : Silica gel (19g), starch (1g), fluorescent indicator (Fluoreszenz-indicator $F_{254}$, Merck, Darmstadt, W. Germany ) (0.06g).

The material is mixed thoroughly in dry state. Water (36ml) is added and the slurry is heated on a water bath with stirring till it becomes more viscous. After cooling, water (2-7 ml) is added to get a mixture suitable for coating TLC plates. Plates are dried at room temperature or at 105°C for 15 min.

Each batch of silica gel is controlled by the separation of dyes (azobenzene, dimethyl yellow, p-methoxy aminobenzene, p-aminobenzene, sudan III) on thin layer.

Silica gel produced should be of high purity.

| | |
|---|---|
| Content of Fe | 0.02% (0.01% on the average ) |
| Residue of benzene extract | 0.02% |
| Residue of ethanol extract | 0.01 % |
| pH of 5% aqueous extract | 6-7 |

## B- PREPARATION OF SILICA GELS WITH LARGE PORE SIZE

All methods used for the production of silica gels enable preparation of microporous materials, i.e of those having an average pore radius from 3-12 nm. By the variation of such parameters as temperature, concentration of starting materials, aging period, etc., the size and distribution of pores can be changed only partially. Silica gel with a large pore size is, therefore, prepared by the modification of a microporous silica gel. Essentially, two methods of microporous silicag gel modification are known. The first one is based on a hydrothermic principle, which involves action of water phase at temperatures 120-300°C and of corresponding vapour pressures. In this way, silica gels with the pore size in the range of 20-500 nm could be prepared. The latter method applies heating of silica gels in the presence of

inorganic salts at the temperatures above 400-700°C.As an inorganic salt $Na_2O$ can be used in the amount of 0.1-10% on the weight of silica gel. Also other inorganic salts as NaCl,$CaCl_2$,$ZnCl_2$,KCl,$NH_4F$ can be used as single additives or in combination.Silica gel is then heated with the aforementioned compounds at 700-1200°C for 5h.

A considerable drawback of all these methods is a long reaction time and very high temperatures.In our experiments,we have used potassium hydrogen sulphate,which has a lower melting point 210°C and gives the same or even better results.Concentration and quantity of potassium hydrogen sulphate solution are selected with respect to pore volume of starting material.

PROCEDURE

Silica gel (100g) is mixed thoroughly with an aqueous solution of $KHSO_4$, which was prepared by dissolving 50g of $KHSO_4$ in 50 ml of hot water (95°C). After drying,the material is heated at 700°C for 1 h.After cooling it is poured into water (500 ml,80°C ) and is mixed for 30 min,filtrated and the filtrate is tested for the presence of $SO_4^{-2}$ ions. Silica gel is finally dried at 120°C.

The following results were obtained :

| | Specific surface area ($m^2/g$) |
|---|---|
| Silica gel S.K (5-40 μm ) | 96.3 |
| Silica gel S.K (40-100 μm ) | 160.6 |
| Silica gel S.K (100-160 μm ) | 63.6 |
| | **Specific pore volume ($cm^3/g$)** |
| Silica gel S.K (5-40 μm ) | 0.58 |
| Silica gel S.K (40-100 μm ) | 0.62 |
| Silica gel S.K (100-160 μm ) | 0.66 |
| | **Average pore radius (nm)** |
| Silica gel S.K (5-40 μm ) | 12.0 |
| Silica gel S.K (40-100 μm ) | 7.2 |
| Silica gel S.K (100-160 μm ) | 20.7 |

By altering the amount of potassium hydrogen sulphate from 30-80% (w/w) on the weight of silica gel,temperature from 600-800°C,and time 1-2h,various grades of silica gel can be prepared.

## FUTURE NEEDS

After successful completion of the project, this Institute will have the basic infrastructure to take up various grades of silica gels which have to be imported at present.

In order to achieve this ojective, it is necessary that all three ion exchange columns are put in operation, optimal conditions for the production of silica gels are established and all necessary equipment is available.

Standardization of specifications: based on the requirements of the country, the specifications of the product used should be standardized. It is the time of compiling a draft monograph of these specifications in consultation with Department of Quality Control and other institutions.

## CONCLUSIONS AND RECOMMENDATIONS

The production of variuos grades of silica gel for chromatography (column, thin and thick layer, GC, HPLC ) has been demonstrated by the consultant at laboratory bench level and also at pilot plant level (production of silica gel itself ) as per availability of apparatus, chemicals, and raw materials. The upscaling activity could not be achieved in all anticipated directions because of delayed shipment and nonavailability of some basic raw materials, chemicals, glass apparatus needed in quantities for carrying out the assignment at the production level desired. The upscaling of these techniques and methodology at regular production level should normally take 1-2 months, after all equipments are in position duly installed.

The expert demonstrated production of silica gel from water glass by ion exchange technology at a pilot plant level. Because of shortage of time, certain limitations and absence of the proper equipment for balancing the optimal conditions the expert does not consider all parameters given to be optimal and they should be found by the staff members in a near future. Nevertheless, under the given conditions and provided that all three ion exchange columns are in operation, a daily production of silica gel is increased more than 9 times in comparison with the present level of production. From the silica gel prepared, three main fractions should be produced according to the partical size :

| | | |
|---|---|---|
| Silica gel with partical size | | 5-40 µm |
| Silica gel | - " - | 40-100 µm |
| Silica gel | - " - | 100-160 µm |

For thin layer chromatography, the expert proposes four basic types of silica gel:

-Silica gel ( 5-40 µm ) - Without additives
-Silica gel $L_{254}$ (5-40 µm) - With fluorescent indicator
-Silica gel G (5-40 µm) - With 13 % of gypsum
-Silica gel $GL_{254}$ ( 5-40 µm ) - With 13% of gypsum and with 0.2-0.5% of fluorescent indicator.

Preparation of all these silica gels has been demonstrated. Futhermore, TLC plates were prepared from silica gel G and silica gel $GL_{254}$. Preparation of TLC plates usin starch as the binder was discussed in detail.

An original method has been demonstrated for the production of large pore size silica gel. For this purpose, an aqueous solution of potassium hydrogen sulphate is mixed with silica gel and heated at 600 - 800°C for 1 - 2 h. By altering the amount of potassium hydrogen sulphate, temperature and time, silica gels with various pore sizes can be prepared. In one experiment, which has been demonstrated, an average pore radius of silica gel samples could be enlarged by 6 times.

Standardization and specification of the silica gels produced is of utmost importance. Due to nonavailability of the special equipment, the expert introduced simple methods for the approximative estimations of specific surface area, specific pore volume and average pore radius of the silica gels produced.

During the present mission, while demonstrating and performing above mentioned experiments, the consultant has observed certain deficiences, keeping in view the future demands of upscaled production of various grades of silica gel.

The consultant therefore recommends as follows.
-To analyze each batch of water glass mainly for $SiO_2$ and $Na_2O$ content
-To find the optimum amount of water glass applied onto the ion exchange column and to establish the optimum flow rate
-To estimate $SiO_2$ and $Na_2O$ concentrations in silicic acid sol.
-To adjust pH of sol to a value optimal for the respective silica gel formation
-To follow aging of gel by pH monitoring
-To follow changes in silica gel structure in drying process

For thin layer chromatography (TLC), the consultant recommends:
-To prepare gypsum of a high purity
-To prepare water soluble starch
-To control each batch of silica gel by dye separation on TLC

-To purchase necessary equipment for coating TLC plates.

-To analyze silica gel for purity as given in the text.

-In order to produce silica gels with various pore sizes,a potassium hydrogen sulphate method should be adapted to the local requirements.

-For standardization and specification of the silica gels produced,the necessary appratus should be available as soon as possible.

-In order to increase a knowledge on silica gel chemistry the book Ralph K.Iler : The Chemistry of silica,Volume I and II,Wiley - Interscience Publication,New York -Chichester - Brisbane - Toronto,should be bought.

-Mrs.Le Minh Nguyet is recommended to spend 3 months at the Institute of Chemistry, Slovak Academy of Sciences,Bratislava,Czechoslavakia with the training programme outlined in Annex II.

ACKNOWLEDGEMENT

The expert acknowledges with sincere thanks :

-The continuous and fruitful co-operation received from Prof.Doan Huy Khac,the National Project Director and Director of the Institute of Drug Quality Control, Hanoi,and from Prof.KTD De Silva CTA of the project.

-The hard and useful work done by the associated research workers Le Minh Nguyet, Ninh Cong Tuyen,Le Kim Loan and assistance of Mrs.Tran Le Sung,Head of Standards and Reagents Section.

-The assistance received from the secretary and interpreter Miss Pham Thu Lan.

The friendly welcome and kind gestures received from all staff members of the Institut

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PROJECT IN THE SOCIALIST REPUBLIC OF VIETNAM

# JOB DESCRIPTION

DP/VIE/84/006/11-89
02

| | |
|---|---|
| Post title | Expert in the Production of Chromatographic Adsorbents |
| Duration | Six weeks |
| Date required | July 1989 |
| Duty station | Hanoi , Vietnam |
| Purpose of project | The strenghening of the Standards and Reagents Section of the Institute of Quality Control to increase its services to the pharmaceutical industry to provide standards, reference substances,reagents and adsorbents both in improved quality and increased quantity to provincial drug quality control institutes,pharmaceutical factories and other public health related institutions. |
| Duties | As a member of international experts assigned to the Institute of Drug Quality Control,under the Chief Technical Adviser and in collaboration with the National Project Co-ordinator, counterpart staff and other international experts, the expert will be expected to:<br>- Train counterpart staff in the production, quality improvement and testing of adsorbents including tlc material with flourescent indicators<br>- Introduce technology for the production of silica gel for use in thin layer chromatography without gypsum<br>- Advise on processes and methods for the production of silica gel of large pore size for use in gas chromatography<br>- Advise on improvements and technologies for the production of microcrystalline cellulose and its derivatives<br>- Recommend processes and methods for increased production of adsorbents and introduction of additional ones.<br>The expert is expected to prepare a final report setting out his findings and recommendations. |

Applications and communications regarding this Job Description should be sent to:

Project Personnel Recruitment Section, Industrial Operations Division
UNIDO, VIENNA INTERNATIONAL CENTRE, P.O. Box 300, Vienna, Austria

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Field of training

Production of standards and reagents for quality control of medicines

| Backstopping Section IO/T/CHEM/PH | Code | Substantive Section IO/T/CHEM/PH | Code | Fellowship Officer | Ext. No | Date issued DD MM YY |
|---|---|---|---|---|---|---|
| Ms. Quintero | J13422 | Ms. Quintero | J13422 | B. Tassew | 3618 | 16/02/89 |

Evaluation: Recommended ☒ 1 Recommended with reservations ☐ 2 Not recommended ☐ 3

Comments:

TO BE COMPLETED BY SUBSTANTIVE SECTION

| Training Programme Outline: | Proposed host institution(s)/Firm(s) | Host country(ies) | Duration |
|---|---|---|---|
| -Different types & grades of Adsorbents, Classification, Quality specifications, activation other modifications and regeneration<br>- Production of various grades of silica gel for chromatography (column, thin and thick layer, HPLC, gas) specifically silica gel H and CH to be used for TLC without gypsum.<br>- Production of silica gel for TLC with fluorescent indicators.<br>- Production of pre-coated silica gel plates or sheets.<br>- Production of large pore size silica gel for gas chromatography.<br>- Production of micro-crystalline cellulose and other derivatives .<br>- Preparation of HPLC plates.<br>- Preparation of silica gel for HPLC columns including reverse phase.<br>- Size reduction, measurement of particle size, porosity and other requisite criteria.<br>- Standard tests and quality control<br>- Sampling, statistical analysis and interpretation of results.<br>- Good Laboratory Practices. Good Manufacturing Practices, Safety in Laboratories specifically dust exhaust systems, maintenance and use of equipment | E. Merck or a suitable Institute working on Adsorbents in West Germany. | West Germany or Czechoslovakia. | 3 mont |

| Reviewing Officer: M. Quintero | Ext. No | Date returned to Training Branch DD MM YY |
|---|---|---|
| Signature: | 3948 | 17/02/89 |

| Total M/M | Estimated max. cost | Placemt. request date DD MM YY | Cleared: Fellowship Officer | Date submitted for computer recording DD MM YY |
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REMARKS: