



Pihak Berkuasa Kawalan Dadah
Drug Control Authority
KEMENTERIAN KESIHATAN MALAYSIA
MINISTRY OF HEALTH MALAYSIA

Rujukan: bil. (74) dlm. BPFK/02/5/1.3
Tarikh: 20/07/07

SEMUA PEMEGANG PENDAFTARAN

Tuan,

FORMULASI BARU 'ORAL REHYDRATION SALTS' (ORS)

Adalah saya dengan hormatnya merujuk kepada surat daripada World Health Organization (WHO) dan United Nations Children's Fund (Unicef) bertarikh 4 Julai 2006 mengenai perkara di atas.

2. Sukacita dimaklumkan bahawa World Health Organization (WHO) dan United Nations Children's Fund (Unicef) telah mengemukakan satu cadangan mengenai formulasi baru yang dipertingkatkan bagi persediaan 'Oral Rehydration Salts' (ORS) yang mana kandungan sodium, glukosa dan osmolariti telah dikurangkan. Salinan surat dari WHO-Unicef tersebut dilampirkan (Silalah rujuk **LAMPIRAN**).

3. Sehubungan dengan itu, semua pemegang pendaftaran produk-produk ORS berdaftar adalah diminta menukar kepada formulasi ORS yang baru tersebut, pihak tuan dikehendaki mengemukakan permohonan dengan menulis surat kepada Setiausaha Pihak Berkuasa Kawalan Dadah (PBKD) dengan menyatakan maklumat-maklumat berikut:

- Nama produk
- No Pendaftaran Produk
- Formulasi asal (bahan-bahan – kuantiti bahan aktif dan eksipien)
- Formulasi baru yang dicadangkan (bahan-bahan – kuantiti bahan aktif dan eksipien, kandungan elektrolit dan glukosa dalam mmol/l)

4. Di samping itu, pemegang pendaftaran terbabit juga akan diminta mengemukakan permohonan variasi bagi formulasi ini dengan mengemukakan semua dokumen yang perlu termasuk 'Batch Manufacturing Formula' (BMF), 'Batch Manufacturing Record' (BMR), label dan sisip bungkusan kepada Unit Variasi, Pusat Pasca Pendaftaran Produk, Biro Pengawasan Farmaseutikal Kebangsaan (BPFK).

5. Pemegang pendaftaran produk adalah diminta mematuhi arahan ini.

Sekian, terima kasih.

" BERKHIDMAT UNTUK NEGARA "
" UTAMAKAN KUALITI, EFIKASI DAN KESELAMATAN "

Saya yang menurut perintah,

(SELVARAJA SEERANGAM)
Setiausaha
Pihak Berkuasa Kawalan Dadah
Kementerian Kesihatan Malaysia.
Imd/HH-110707-Pekeliling/2007

s.k

- Pengarah Perkhidmatan Farmasi, Program Perkhidmatan Farmasi, KKM.
- Pengarah Biro Pengawasan Farmaseutikal Kebangsaan, KKM.
- Ketua Pusat Pembangunan Organisasi (PPO), BPFK.
- Ketua Pusat Pasca Pendaftaran Produk (PPPP), BPFK.
- Pharmaceutical Association of Malaysia (PhAMA).
- Persatuan Industri Farmaseutikal Malaysia (MOP!).
- Presiden, Majlis Perubatan Homeopathy Malaysia.
- Presiden, Federation of Chinese Physicians & Medicine Dealers Association Malaysia (FCPMDAM).

LAMPIRAN

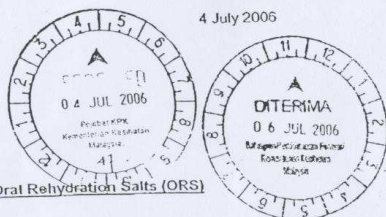


4 July 2006

Tan Sri Datuk Dr Haji Mohd Ismail Merican
Director General
Ministry of Health
Putrajaya

Dear Tan Sri Datuk,

New Improved Oral Rehydration Salts (ORS)



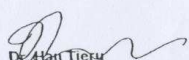
In the spirit of sharing the latest technical information on Oral Rehydration Salts (ORS) and treatment of diarrhea, we would like to present to you a joint WHO-UNICEF letter on the revision of the recommended composition of ORS.

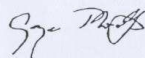
With respect to the ORS being presently distributed in Malaysia, we would appreciate your esteemed assistance in distributing the attached letter to manufacturers whose product is available in Malaysia.

If you would like any further information on this subject, please feel free to contact the WHO or UNICEF country office.

We take this opportunity to assure you of our highest considerations.

Yours sincerely,


Dr. Han Tien
WHO Representative
For Brunei Darussalam, Malaysia
& Singapore


Gaye Phillips
UNICEF Representatif

Cc Dato' Dr. Dato' Dr. Shafie bin Ooyub, Deputy Director-General (Public Health), Ministry of Health, Malaysia

Dato' Dr Abdul Gani bin Mohamed Din, Deputy Director-General (Medical)
Ministry of Health, Malaysia

Datuk IR Dr M S Pillay, Deputy Director-General (Research & Technical Support),
Ministry of Health Malaysia

Datuk Dr Haji Ramlee bin Haji Rahmat, Director, Disease Control Division
Ministry of Health, Malaysia



13 May 2005

Dear Sir/Madam,

New Improved Oral Rehydration Salts (ORS)

Diarrhoea continues to be a major cause of childhood mortality, with 1.6 million children under five years of age dying every year from diarrhoea. The United Nations Children's Fund (UNICEF) and the World Health Organization (WHO) have since the 1970s promoted the use of Oral Rehydration Salts (ORS) for the management of diarrhoea. It is estimated that during the 1990s more than 1 million diarrhoea-related deaths have been prevented each year, largely through the promotion and use of Oral Rehydration Therapy (ORT).

Recent advances in managing diarrhoeal disease, including the newly formulated low osmolarity ORS containing lower concentration of glucose and salt, can drastically reduce the number of child deaths. This new ORS shortens the duration of diarrhoea and reduces the need for unscheduled intravenous fluids.

UNICEF and WHO have called upon countries to improve the availability of the new ORS solution, through both private and public channels. The commercial sector is a critical partner, working closely with the public sector, in ensuring that the newly formulated ORS is made available to communities and households as soon as possible.

UNICEF and WHO are appealing to all companies now producing ORS to switch production to the newly recommended ORS formulation. WHO guidelines for this new formulation are enclosed.

The new ORS is recommended for treatment of dehydration due to diarrhoea in both children and adults. Samples of ORS sachets are available from UNICEF Supply Division in Copenhagen*. Each new formulation ORS sachet contains the following:

Glucose anhydrous Food Grade:	13.5 gm
Sodium chloride BP98:	2.6 gm
Trisodium citrate dehydrate BP98:	2.9 gm
Potassium chloride BP98:	1.5 gm
Net wt:	20.5 gm

*UNICEF Supply Division, UNICEF Plaza, Copenhagen OE, Denmark
Telephone: 45 33 273 5277, Facsimile: 45 33 269 221

It is recommended that the contents of each sachet be dissolved in one litre of drinking water:

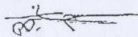
- Infants - one litre over a 24 hour period.
- Children over one year - one litre over an 8 to 24 hour period according to age.
- Adults - drink freely as required.

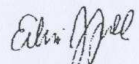
Families and communities will be important partners in achieving the goals set for managing diarrhoeal disease by making the new recommendations routine practice in the home as well as in the health facility.

Besides the new ORS, the recently published "Joint WHO/UNICEF Statement on the Clinical Management of Acute Diarrhoea" also calls for using zinc supplementation in the management of diarrhoea. Zinc supplementation can further reduce the duration and severity of the diarrhoea episode as well as lower the incidence of diarrhoea in the following two to three months. A copy of the Joint Statement is enclosed for your information.

UNICEF and WHO welcome the ongoing commitment from the commercial sector to support countries to quickly reduce deaths due to diarrhoea and to help achieve the Millennium Development Goal of reducing the under-five mortality rate by two thirds by the year 2015. Producing the new, low osmolarity ORS is an important contribution.

Yours sincerely,


Joy Phumaphi
Assistant Director-General
Family and Community Health
World Health Organization
20 Avenue Appia
1211 Geneva 27


Edwin J. Judd
Director
Programme Division
United Nations Children's Fund
3 United Nations Plaza
New York
New York 10017



WHO



unicef

ORAL REHYDRATION SALTS (ORS) A NEW REDUCED OSMOLARITY FORMULATION

For more than 25 years WHO and UNICEF have recommended a single formulation of glucose-based Oral Rehydration Salts (ORS) to prevent or treat dehydration from diarrhoea irrespective of the cause or age group affected. This product, which provides a solution containing 90 mEq/l of sodium with a total osmolarity of 311 mOsm/l, has proven effective and without apparent adverse effects in worldwide use. It has contributed substantially to the dramatic global reduction in mortality from diarrhoeal disease during the period.

For the past 20 years, numerous studies have been undertaken to develop an "improved" ORS. The goal was a product that would be at least as safe and effective as standard ORS for preventing or treating dehydration from all types of diarrhoea but which, in addition, would reduce stool output or have other important clinical benefits. One approach has consisted in reducing the osmolarity of ORS solution to avoid possible adverse effects of hypertonicity on net fluid absorption. This was done by reducing the solution's glucose and salt (NaCl) concentrations.

Studies to evaluate this approach were reviewed at a consultative technical meeting held in New York (USA) in July 2001¹, and technical recommendations were made to WHO and UNICEF on the efficacy and safety of reduced osmolarity ORS in children with acute non-cholera diarrhoea, and in adults and children with cholera.

These studies showed that the efficacy of ORS solution for treatment of children with acute non-cholera diarrhoea is improved by reducing its sodium concentration to 75 mEq/l, its glucose concentration to 75 mmol/l, and its total osmolarity to 245 mOsm/l. The need for unscheduled supplemental IV therapy in children given this solution was reduced by 33%. In a combined analysis of this study and studies with other reduced osmolarity ORS solutions (osmolarity 210-268 mOsm/l, sodium 50-75 mEq/l) stool output was also reduced by about 20% and the incidence of vomiting by about 30%¹. The 245 mOsm/l solution also appeared to be as safe and at least as effective as standard ORS for use in children with cholera.

The reduced osmolarity ORS containing 75 mEq/l sodium, 75 mmol/l glucose (total osmolarity of 245 mOsm/l) is as effective as standard ORS in adults with cholera. However, it is associated with an increased incidence of

¹ Reduced osmolarity oral rehydration salts (ORS) formulation - Report from a meeting of experts jointly organized by UNICEF and WHO, WHO/CHEG-22
http://www.who.int/child-adolescent-health/New_Publications/CHILD_HEALTH/Expert_consultations.htm

transient, asymptomatic hyponatraemia. This reduced osmolarity ORS may be used in place of standard ORS for treating adults with cholera, but careful monitoring is advised to better assess the risk, if any, of symptomatic hyponatraemia.

Because of the improved effectiveness of reduced osmolarity ORS solution, especially for children with acute, non-cholera diarrhoea, WHO and UNICEF now recommend that countries use and manufacture the following formulation in place of the previously recommended ORS solution with a total osmolarity of 311 mOsm/l.

Reduced osmolarity ORS	grams/litre	Reduced osmolarity ORS	mmol/litre
Sodium chloride	2.6	Sodium	75
Glucose, anhydrous	13.5	Chloride	65
Potassium chloride	1.5	Glucose, anhydrous	75
Trisodium citrate, dihydrate	2.9	Potassium	20
		Citrate	10
		Total Osmolarity	245

Although this single ORS formulation is *recommended*, WHO and UNICEF have previously published criteria, which remain unchanged, for *acceptable* ORS formulations. These criteria are listed below; they specify the desired characteristics of the solution after it has been prepared according to the instructions on the packet:

The total substance concentration	(including that contributed by glucose) should be within the range of 200-310 mmol/l
The individual substance concentration	
Glucose	should at least equal that of sodium but should not exceed 111 mmol/l
Sodium	should be within the range of 60-90 mEq/l
Potassium	should be within the range of 15-25 mEq/l
Citrate	should be within the range of 8-12 mmol/l
Chloride	should be within the range of 50-80 mEq/l

At UNICEF Supply Division, a bid for Reduced Osmolarity ORS was launched in September 2003 and two manufacturers were approved for the supply of new ORS formulation. The new ORS is in stock at UNICEF Supply Division. Phase out of the old ORS and phase in of the new ORS is taking place and the old ORS will for a short period of time be part of the New Emergency Health Kit, as a certain stock of these kits have been packed before the introduction of the new ORS. For the moment, the price of new ORS is approximately 15% lower than the old ORS formulation.

The material numbers will change as follows, as the new formulation will replace the existing ORS:

- ORS, 1L sachet/Box-100 from 1561110 to 1561120
- ORS, 1L sachet/CAR-1000 from 1561111 to 1561121

If you have any questions regarding procurement/supply, please contact:

Christine Brandt
Technical Assistant
UNICEF Supply Division
Tel: +45 35 27 30 15
Email: cbrandt@unicef.org

If you have any questions regarding case management of diarrhoea, please contact:

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