IAHPC List of Essential Medicines for Palliative Care
Summary of Process for Editors of Pain and Palliative Care Journals

Background
The World Health Organization (WHO) Cancer Control Program requested the support from the International Association for Hospice and Palliative Care (IAHPC) to develop a list of essential medicines for palliative care. The current WHO Model List of Essential Medicines has a section called Palliative Care, which does not list any medications, but the following statement:

Section 8.4 - Medicines used in palliative care
The WHO Expert Committee on the Selection and Use of Essential Medicines recommended that all the drugs mentioned in the WHO publication Cancer Pain Relief: with a Guide to Opioid Availability, second edition, be considered essential. The drugs are included in the relevant sections of the Model List, according to their therapeutic use, e.g. analgesics.

The request from WHO was to prepare a list based on the recommendation from palliative care experts, taking in consideration two criteria: Efficacy and Safety. The WHO will be carrying out the Cost Effectiveness analysis and evidence based reviews of the recommended medications.

To work on this proposal, IAHPC formed a working committee which included board members of IAHPC and external advisors from the field. The group was chaired by Dr. Neil MacDonald and co-chaired by Dr. Carla Ripamonti. Other members included Doctors Kathy Foley, Eduardo Bruera, David Currow and Ms. Liliana De Lima. Doctors Peter Glassman and Karl Lorenz served as expert advisors. The Committee developed a plan of action, which included the following steps:

1. **Identifying the most prevalent symptoms in palliative care**.
   After several discussions among the committee members, it was agreed that the best approach to build a list was to start with a list of the most common symptoms in palliative care. It was also agreed that the group would focus on symptoms and not the treatment of underlying conditions, therefore the treatment of diseases such as cancer, HIV and other infections were excluded.
   An initial list of the 21 most common symptoms in palliative care was developed by the committee. These are included in Table 1.

2. **First List: Identifying the medications used to treat these symptoms**:
   - IAHPC board members and other palliative care leaders from around the world were asked to propose appropriate medications for these symptoms identified in Step one.
   - Of a total of forty, thirty-four physicians responded (85%), 15 from developing countries. In total they recommending 147 products. This initial list was decreased to 120 by removing non medications (i.e. oxygen and vitamins) and duplicates.

3. Second List: Online survey and modified Delphi process
   - An online survey of 19 rating panels (one for each symptom and four for pain: mild to moderate; moderate to severe; visceral pain and bone pain) was sent by email to 112 physicians and pharmacologists (77 from developing countries).
   - Using a scale of 1-9, participants were asked to rate the safety and efficacy of each medication and were given the following definitions:

a. Effectiveness: *A drug class or medication is defined as effective for treating a specific symptom in a palliative care population based on consideration of:*
Evidence of Treatment Effectiveness: The strongest evidence is derived from randomized controlled trials (RCTs), but other experimental designs, observational studies, and expert opinion are also useful in rating this issue in the absence of RCTs. With respect to drug class, the evidence should be consistent across drugs within a group.
Ratings of 1-3 mean that the drug class or medication is not effective for treating that specific symptom in palliative care populations; ratings of 4-6 mean that there will be considerable variability in the effectiveness of that drug class or medication for treating that specific symptom in palliative care populations; and ratings of 7-9 mean that drug class or medication is very effective for treating that specific symptom.

b. Safety: *the safety profile of an agent, when used in a clinically appropriate manner, is sufficiently known (and/or described) in the target and/or general population so that adverse events can be anticipated and, if possible, prevented; or, when they occur, can be duly recognized and mitigated. In addition, the safety profile of one agent should be viewed in context of its pertinent comparators.*
Ratings of 1-3 mean that drug class or medication is not safe for use in palliative care populations; ratings of 4-6 mean that there will be considerable variability in the safety of using a drug class or medication in palliative care populations; and ratings of 7-9 mean that the drug class or medication is very safe to use in this population.

- Seventy one participants (63%) responded the modified Delphi survey.
- Results from the modified Delphi survey indicated there was little consensus among the respondents to recommend medications as both safe and effective for 5 of the 23 symptoms: Bone pain, dry mouth, fatigue, hiccups and sweating.

4. Final List

- Twenty eight global, regional and professional organizations working in pain and palliative care were invited to a meeting in Salzburg, Austria on April 30th to May 2nd, 2006. Thirty one representatives from 26 of these organizations attended. Table 2 includes the list of participants and organizations represented in the meeting.
- A few initial presentations were given to the group, including from the WHO representatives about the Model List, the use and access to controlled substances, the process of selecting a formulary for the Veteran's Administration Hospital in the USA and the process of developing a model list for palliative care for the country in Australia.
- A set of principles to guide the discussions and the meeting were also presented. These outlined ethical principles and the importance of maintaining a global approach during our discussions so that our decisions would be applicable in all countries of the world. Annex 1 includes the principles.
- Participants received a copy of the current WHO Model List of Essential Medicines and the results of the Delphi survey.
- Participants were split among three working groups. Each was assigned a chair to lead the discussions. The groups and their corresponding chairs were:
    - Medications used to treat mental health symptoms – Luigi Grassi
    - Medications to treat pain – Franco De Conno
    - Medications to treat gastrointestinal symptoms – James Cleary
- A few "orphan" symptoms (i.e. hiccups) were randomly assigned to each group.
- Each group proceeded to discuss and select among the medications with the highest ratings in the Delphi survey, those they considered essential for each symptom.

- The chairs shared the results with the rest of the participants.
- The combined group reviewed and discussed the list proposed by each group. When there were differences in the opinions of the participants, the group discussed the alternatives and the best option was decided by consensus. Through this process, each one of the recommended medications was reviewed and if agreed among the whole group, it was included in the IAHPC List.
- The final list of medications was approved by the participants as the IAHPC Essential Medicines List for Palliative Care which is included in the attached spread sheet. The third column describes the IAHPC indication for palliative care and the fourth column identifies those medications which are already included in the WHO Model List of Essential Medicines as well as the treatment indications by WHO.
- The group agreed with the respondents of the survey in that there is not enough evidence to recommend any medications as both safe and effective for five of the symptoms: Bone pain, dry mouth, sweating, fatigue and hiccups and recognized that additional research is needed to identify safe and effective medications to treat these symptoms.
- The IAHPC list includes 33 medications of which 14 are already included in the WHO list as essential in the treatment of several conditions, some of which are common in palliative care. The inclusion of a medication in one section of the WHO list does not preclude its inclusion in a different section, if the medication is determined by WHO to be essential for the treatment of different conditions.

5. Future

- IAHPC has decided to give the list to editors in different journals and provide them with the first opportunity to disseminate the list.
- After the list has been published in different journals, IAHPC will ask organizations, institutions and individuals to help disseminate and promote the list. They are free to use, adapt, change and improve the list to fit the needs of their patients.
- IAHPC encourages countries to use this list as a model and develop their own list of medications for Palliative Care, tailored to meet the needs of their patients and taking into account their own resources and medications available.
- IAHPC encourages additional debate and discussion to move this list forward, improve it and find ways to improve the access to medications.
- IAHPC will prepare a full report of the process and publish it as a chapter in the next edition of the Oxford Textbook of Palliative Medicine.

Table 1 – Most Common Symptoms in Palliative Care

Pain: Mild to Moderate Moderate to Severe Bone Neuropathic Visceral	
Dyspnea	Fatigue
Terminal Respiratory Congestion	Anxiety
Dry mouth	Depression
Hiccups	Delirium
Anorexia-cachexia	Insomnia
Constipation	Terminal Restlessness
Diarrhea	Sweating
Nausea	
Vomiting	

Table 2 – Organizations represented in the Salzburg Meeting

NAME	Representing	Country
Adams, Vanessa	Velindre NHS Trust and Hospice Africa Uganda	UK and Uganda
Alexander, Carla	National Association for Palliative Care (NHPCO)	USA
Aapro, Matti	Multinational Ass. For Supportive Care in Cancer (MASCC)	Switzerland
Callaway, Mary	International Palliative Care Initiative - Open Society Institute	USA
Cleary, Jim	American Academy of Hospice and Palliative Medicine (AAHPM)	USA
Daeninck, Paul	Canadian Society of Palliative Care Physicians	Canada
De Conno, Franco	European Association for Palliative Care (EAPC)	Italy
Doyle, Derek	National Council for Palliative Care	UK
Filbert, Marilene	European Association for Palliative Care (EAPC)	France
Foley, Kathy	International Palliative Care Initiative - Open Society Institute	USA
George, Reena	Christian Medical College, Vellore	India
Glassman, Peter	USA Veterans' Administration Medical Center	USA
Goh, Cynthia	Asia Pacific Hospice Palliative Care Association (APHN)	Singapore
Grassi, Luigi	International Psycho Oncology Society (IPOS) and World Psychiatric Association	Italy
Gwyther, Elizabeth	Hospice and Palliative Care Association of South Africa (HPCA)	South Africa
Hanks, Geoffrey	International Assoc. for the Study of Pain (IASP)	UK
Krakauer, Eric *(rapporteur)*	Vietnam CDC, Harvard Medical School AIDS Partnership (VCHAP)	USA
Law, Freida	Li Ka Shing Foundation	China
Luczak, Jacek	Eastern and Central Europe Palliative Care Task Force	Poland
Merriman, Anne	African Palliative Care Association	Uganda
Praill, David	Help The Hospices	UK
Rowett, Debra	Palliative Care Australia	Australia
Rubach, Maryna	European Society of Medical Oncology	Poland
Serdar, Erdine	European Federation of IASP Chapters (EAFIC)	Turkey
Wenk, Robert	Latin America Association for Palliative Care (ALCP)	Argentina
IAHPC		
MacDonald, Neil *(Chair)*	International Association for Hospice & Palliative Care (IAHPC)	Canada
Ripamonti, Carla *(Co-Chair)*	International Association for Hospice & Palliative Care (IAHPC)	Italy
DeLima, Liliana *(Coordinator)*	International Association for Hospice & Palliative Care (IAHPC)	USA
WHO (as observers)		
Hill, Suzanne	WHO - Dept of Medicines Policy and Standards	Switzerland
Scholten, Willem	WHO - Dept of Medicines Policy and Standards	Switzerland
Sepulveda, Cecilia	WHO – Cancer Control Program	Switzerland

Annex 1
IAHPC List of Essential Medicines for Palliative Care
Principles
by Derek Doyle – founding member and adviser, IAHPC

The *IAHPC Essential Medicines List for Palliative Care* has been produced by a representative group of palliative care specialists, each with very considerable experience in this discipline. Some work in countries where palliative care is well established and developing rapidly, others in countries at earlier stages of development. They come from countries differing in the sophistication of their health care provision, culture, ethnic, linguistic and religious traditions. They are each affiliated to, and represent, national and international associations and societies for the study and provision of palliative care.

These palliative medicine specialists share a commitment to the provision of palliative care to who all need it irrespective of race, colour, creed, class or financial means. They believe that

- Every person with a life threatening illness has the right to receive appropriate palliative care
- It is the responsibility of every clinician to provide appropriate palliative care to those who need it.
- That patients receiving palliative care should be enabled to receive it in the place of their choice.

The *IAHPC Essential Medicines List for Palliative Care* is not a directive but is offered for guidance. Important as the cost of medicines is in every country, the list is not based on cost, which must be calculated nationally.

The *IAHPC Essential Medicines List for Palliative Care* has been produced with only one aim – the provision of the best possible care for those with advanced life-threatening illness, uninfluenced by financial and other benefits or political considerations..

The *IAHPC Essential Medicines List for Palliative Care* will be of little use if

- Physicians and students are not taught how to use these medicines in the palliative care setting
- The medicines are not made available and accessible, if needs be by appropriate legislation
- The *List* is not brought to the attention of physicians and pharmacists by relevant government, professional and academic bodies, professional journals and charities involved in promotion and supporting the provision of palliative care
- Countries do not have in place, or are prepared to produce, National Palliative Care Policies / Guidelines.

The *Essential Medicines List for Palliative Care* is not an endorsement of any product does not assume similar pharmacological action or adverse effects and should not be read as promoting a proprietary preparation.

The *IAHPC Essential Medicines List for Palliative Care* will need to be reviewed and revised on a regular basis, taking into account research findings, changes in practice and constructive comments from palliative car workers worldwide.

The following principles flow from the points listed above:

Every effort should be made to ensure ready availability and accessibility of all essential medicines before approving more expensive but equally efficacious formulations.

Every effort should be made to ensure that prescribing physicians and pharmacists are made aware of comparative costs of drugs on the essential medicines list and their more expensive competitors with equivalent therapeutic benefit. [This can only be done at national rather than international level]

Every encouragement should be given to editors of scientific and in particular palliative care, journals to encourage the publication of the essential medicines list for palliative care.

Every effort should be made to get charities supporting palliative care to encourage recipients of their funds to use the drugs on the essential medicine list in preference to more expensive ones with equivalent therapeutic benefit.

All trainees in palliative care – whether medical, nursing, pharmacy, clinical psychology – should be made aware of the *IAHPC Essential Medicines List for Palliative Care,* should expect to be examined on it, and understand why drugs were selected for the list.

The *IAHPC Essential Medicines List* should be brought to the attention of the groups being set up in many countries to keep politicians informed about palliative care so that they may learn of the benefits of such a list, of the pressing need for legislation to establish availability and accessibility of the medicines, and know what is being done in other countries to promote and provide palliative care to all who need it, irrespective of race, creed, or financial means.

The *IAHPC Essential Medicines List for Palliative Care* should be studied by all the national and international professional associations and societies represented by the specialists who have drawn it up, and their considered opinions and suggestions on it, taken into account when the list is finalized and subsequently kept up-to-date.

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