WHO Guidelines on Public Health Response to Radiation Emergencies

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OUTLINE

• Introduction
• IHR implementation and Joint External Evaluation framework
  – JEE tool
  – JEE process
• Technical tools development
  – Public health response guidelines
  – Iodine thyroid blocking recommendations
  – National KI policy survey
• Capacity building activities
Framework for WHO Response to RN Emergencies

- WHO Constitution 1948 and relevant World Health Assembly Resolutions
- International Health Regulations (2005)
- Conventions on Early Notification and Assistance (1987)
  - Inter-Agency Committee for Radiological and Nuclear Emergencies (IACRNE) and Joint Plan
- Partnerships and collaboration
  - External partners (IOs, national authorities, relevant stakeholders)
  - WHO expert networks (REMPAN, BioDoseNet, INFOSAN, EOC-NET, etc.)
  - WHO Collaborating Centers
WHO REMPAN

- A WHO technical expertise arm for providing to MS assistance on strengthening national capacities, access to technical expertise and information sharing platform
- comprises 40+ member institutions and individual experts in 40 countries
- meets every three years
- proceedings published in peer-review journals
- Directory is available on the web:

http://www.who.int/ionizing_radiation/a_e/rempan/en/
New!!!
Proceedings of the 14th REMPAN meeting that took place in Wuerzburg, Germany in May 2014 were published in the Special Issue of the RPD in August 2016
Strengthening Preparedness in MS

- Supporting the IHR implementation by member states
  - Implementing Global Health Security Agenda
  - conducting Joint External Evaluation missions (JEE)
- Developing and supporting implementation of the international norms and standards
  - contribution to relevant IAEA's requirements, guides, etc.
  - developing technical guidelines for health sector
- Promoting international cooperation in the EPR area through two global expert networks REMPAN and BioDoseNet
- Engaging in the research agenda for medical countermeasures development and epidemiological studies
IHR Implementation and Joint External Evaluation (JEE)
International Health Regulations (2005)

- **Legally binding treaty**
- **196 States Parties**
- **In force 15 June 2007**

States must prepare, report and cooperate

WHO must coordinate

http://www.who.int/ihr/about/en/
IHR Monitoring Post 2015

- Recommendations of the IHR-Review Committee (November 2014) endorsed by the Resolution WHA68.5 (2015)

- Global formal consultative process involving MS through the Regional Committee Meetings in 2015, and the 69th WHA in May 2016.

- WHO proposed a Monitoring & Evaluation Framework that represents a shift from exclusive self assessment to a combined methodological approach that includes an external evaluation.
New Combined approach – Four Components

- Annual Reporting
  - Transparency
  - Mutual accountability
- After Action Review
  - Trust building
  - Appreciation of public health benefits
- Exercises
  - Dialogue
- Joint External Evaluation
  - Sustainability
Joint External Evaluation of IHR implementation

- Developed in collaboration with partners and initiatives such as the Global Health Security Agenda (GHSA), the JEE tool and process is a part of the IHR (2005) Monitoring and Evaluation framework (http://www.who.int/ihr/publications/WHO_HSE_GCR_2016_2/en/)

- Since March 2016, the JEE reviews were done in 11 countries, including Pakistan, Turkmenistan, Qatar, Morocco, USA, etc.

- Focuses on health security and cross-sector coordination and includes 19 areas of evaluation, radiation emergencies being one of them.

- Somewhat similar to EPRev but not as thorough and detailed at the technical level as EPRev, however – we need to find the way to coordinate these two mechanisms.
Joint External Evaluation missions (JEE)

As of Nov 2016, 21 JEE missions completed in six WHO regions:

- **AMRO** – 1 country
- **AFRO** – 6 countries
- **EURO** – 3 countries
- **EMRO** – 7 countries
- **SEARO** – 1 country
- **WPRO** – 2 countries

![Map of the World showing JEE missions in different WHO regions.](image)
Joint External Evaluation Missions
Direct support from GHSA
Information Sharing

• Once the evaluation report is finalized – it will be published in WHO IHR portal https://extranet.who.int/ihrportal/ and/or WHO Strategic Partners Portal https://extranet.who.int/donorportal/

• Government can published their report on the Ministry of Health website

• Partners can publish their reports on their respective website as per the country concurrence
A proposal for EPReSC

• To seek feedback on JEE tool from EPReSC
• To include a more detailed report on JEE process and results in the agenda of EPReSC-4
• To discuss how JEE process can be aligned with EPRev process to:
  – avoid duplication
  – ensure consistency
  – synergize the efforts of both agencies
Technical tools development
Relevant international publications

• Safety requirements: BSS – GSR Part 3 (2011) and GSR Part 7 (2015), cosponsored by WHO among other IOs

• Arrangements for preparedness for a nuclear or radiological emergency, GS-G-2.1, cosponsored by FAO, IAEA, ILO, PAHO, OCHA and WHO (2007)

• Criteria for use in preparedness and response for a nuclear or radiological emergency, cosponsored by FAO, IAEA, ILO, PAHO, OCHA and WHO, GSG-2 (2011)

• Actions to protect the public in an emergency due to severe conditions at a light water reactor (EPR-NPP 2013)

• Generic Procedures for medical response during a nuclear or radiological emergency, cosponsored by WHO (EPR Medical 2005)
Development of Guidelines on Public Health Response to Radiation Emergencies

- Requested by MS in the aftermath of Fukushima accident in 2011
- Scoping survey of MS in 2012 demonstrated the need among public health authorities for guidelines on PH aspects of the response to radiation emergencies.
- Funding was provided by the governments of Japan (MoH) and Switzerland (SFOPH), and for the ITB component – by Germany (BMUB, in kind) and Australia (ARPANSA).
- Methodology is described in WHO Handbook for developing guidelines: www.who.int/kms/guidelines_review_committee/en/
Development of Guidelines on Public Health Response (PHR) to Radiation Emergencies

- Guidelines Development Group (GDG) meetings took place:
  - 1\textsuperscript{st} GDG meeting in Geneva, June 2012 identified the scope, methods of work, developed project work plan and defined research questions
  - 2\textsuperscript{nd} meeting in Amman, Jordan in June 2013, reviewed, evaluated and graded the evidence base and derived recommendations by using special matrix tool
  - 3\textsuperscript{rd} meeting was held by Webex to address additional research questions
  - 4\textsuperscript{th} meeting in Wuerzburg, Germany in May 2014 to focus specifically on thyroid iodine blocking (ITB)
  - 5\textsuperscript{th} meeting in Pisa, Italy in January 2016 to derive recommendations on ITB
- IAEA participated in some of the meetings as observer
PHR Guide Project

- To assist MS in building national capacities for PH preparedness and response to radiological and nuclear emergencies, WHO is developing a new technical tool - A Guide for Public Health Response (PHR) to Radiological and Nuclear Emergencies, using the standard format and quality criteria required by WHO policy on guidelines development.

- These guidelines aim to support national policy and decision making by national public health authorities as a complementary tool to the existing international safety requirements and guides.

The content is developed by independent technical experts in the field under the guidance and governance of WHO Secretariat and Internal Steering Group.
Research areas included in the scope of systematic reviews

- Evacuation of the general public
- Evacuation versus sheltering in combination with iodine thyroid blocking (ITB)
- Iodine thyroid blocking (age and timing requirements, risk of side-effects)
- Monitoring and decontamination of general public
- Monitoring of food and drinking water safety
- Cessation of emergency interventions and transition to existing exposure situation
- Identification of people who should be included and methods for long-term health surveillance
- Crisis communication
Guidelines development process at WHO: transparency, quality assessment, bias reduction

1. Scoping the document

2. Setting up Guideline Development Group and External Review Group
   - 2010

3. Management of Conflicts of Interest
   - 2013

4. Formulation of the questions (PICOT), choice and rating of the relevant outcomes
   - 2013-14

5. Evidence retrieval, assessment and synthesis (systematic review(s)
   - 2014

   - GRADE - evidence profile
   - 2015

6. Formulation of the recommendations (GRADE)
   - 2016

   - Including explicit consideration of: Benefits and harms, Values and preferences, and Resource use

7. Dissemination, implementation (adaptation)

8. Evaluation of impact

9. Plan for updating

Drafting and peer-review
Grades of Recommendation Assessment, Development and Evaluation

• Emphasizes:
  – Systematic approach
  – Explicitness
  – Transparency
  – Quality of evidence
  – Patient important outcomes

• Uses standardized Evidence-to-Recommendation matrix tables (E-2-R) to present:
  – Summary of evidence (evidence profile)
  – The factors that affect the final recommendation (decision table)

www.gradeworkinggroup.org
GRADE is adopted by more than 90 organizations!!!
<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Design</th>
<th>Quality assessment</th>
<th>Number of patients</th>
<th>Effect</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Limitations</td>
<td>Inconsistency</td>
<td>Indirectness</td>
<td>Imprecision</td>
</tr>
<tr>
<td>ATMA</td>
<td>Cross-sectional study</td>
<td>Serious concern</td>
<td>No serious concern</td>
<td>No serious concern</td>
<td>Very serious concern</td>
</tr>
<tr>
<td></td>
<td>TgAB</td>
<td>Cross-sectional study</td>
<td>Serious concern</td>
<td>No serious concern</td>
<td>No serious concern</td>
</tr>
<tr>
<td>Thyroid Cancer</td>
<td>Analytic cohort study</td>
<td>No serious concern</td>
<td>No serious concern</td>
<td>No serious concern</td>
<td>Serious concern</td>
</tr>
<tr>
<td></td>
<td>Case-control study</td>
<td>Serious concern</td>
<td>Serious concern</td>
<td>No serious concern</td>
<td>Serious concern</td>
</tr>
</tbody>
</table>
Factors determining strength of recommendation

- Priority of the problem
- Quality of evidence
- Balance of benefits and harms
- Values and preferences
- Resource use
- Equity
- Feasibility
- Acceptability

All these factors must be included in the process of deriving recommendations.
### ITB Evidence-to-Recommendation matrix

#### Evidence to Recommendation framework

**Should KI be administered vs. not administered to people exposed to radiiodine release in the environment in the setting of radiological or nuclear emergency?**

**Population:** People exposed to radiiodine release in the environment  
**Intervention:** KI administration  
**Comparison:** No KI administration  
**Setting:** radiological or nuclear emergency  
**Perspective:** public health

**Background:** to include types of emergencies  

**Subgroup considerations:** children and adolescents 0-18, pregnant and breast-feeding women, elderly

<table>
<thead>
<tr>
<th>CRITERIA</th>
<th>JUDGEMENTS</th>
<th>RESEARCH EVIDENCE</th>
<th>ADDITIONAL CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Is the problem a priority?</strong></td>
<td>No Yes</td>
<td>Incidence of thy ca: low background incidence, rare disease</td>
<td>Public perception of childhood thy ca and nuclear accidents:</td>
</tr>
<tr>
<td></td>
<td>No Yes</td>
<td>Strong association with radiodines exposure and increased risk of thy ca for</td>
<td>- Chernobyl experience</td>
</tr>
<tr>
<td></td>
<td>No Yes</td>
<td>persons exposed at the age 0-18 (Chernobyl studies)</td>
<td>- Fukushima experience (Lancet paper on psychological impact – Ari Hasigawa)</td>
</tr>
<tr>
<td></td>
<td>No Yes</td>
<td>Brenner study - ref</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No Yes</td>
<td>Cardis study – ref</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No Yes</td>
<td>Zaboltskaya study – ref</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No Yes</td>
<td>Range of risk estimates</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No Yes</td>
<td>Risk is higher for iodine deficient areas (PV to send ref)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No Yes</td>
<td>Some indications for radiation-induced thy ca being more aggressive than</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No Yes</td>
<td>spontaneous thy ca (PV – ref?)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No Yes</td>
<td>Quality of life issue, burden of management issue (CR - ref?)</td>
<td></td>
</tr>
</tbody>
</table>

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The 3rd Meeting of EPReSC – 01 Dec 2016 – Vienna, Austria
## ITB Evidence-2-Recommendation matrix

<table>
<thead>
<tr>
<th>CRITERIA</th>
<th>JUDGEMENTS</th>
<th>RESEARCH EVIDENCE</th>
<th>ADDITIONAL CONSIDERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>How large are the resource requirements?</td>
<td>Large costs</td>
<td>Kenigsberg’s paper on Chernobyl KI costs – in Russian (ZC to check)</td>
<td>Resources: KI stockpile acquisition, disposal and renewal, storage, education for public and heal-care providers, communication campaign, logistics of distribution/pre-distribution. Saved costs: thy ca management</td>
</tr>
<tr>
<td>How large is the incremental cost relative to the net benefit?</td>
<td>Very large</td>
<td>No actual evidence (check Kenigsberg paper)</td>
<td>Here judgement applies to the stockpile/supply of KI, rather than administering KI, as latter requires to have a stockpile in place. Considering risk of a severe nuclear accident 1 in 10,000 reactor-year (LxB – ref), the cost-effectiveness of KITB may be low. From a health policy maker’s perspective, KITB cost-effectiveness may be higher, since KI costs is low.</td>
</tr>
<tr>
<td>What would be the impact on health inequities?</td>
<td>Increased</td>
<td>No actual evidence</td>
<td>The issue relates to pre-distribution choice, which varies from country to country. Pre-distribution is not explicitly included in the scope of this guideline, however, having a comprehensive national programs on EPR planning would lead to increased equity</td>
</tr>
<tr>
<td>Is the option acceptable to key stakeholders?</td>
<td>No</td>
<td>No actual evidence</td>
<td>Stakeholders: policy makers, emergency response agencies, public, health-care professionals, nuclear operators, nuclear safety authorities, radiation protection authorities, researchers/academia, KI manufacturers, risk communicators, etc.</td>
</tr>
<tr>
<td>Is the option feasible to implement?</td>
<td>No</td>
<td>Polish evidence, Fukushima experience?</td>
<td>In general, KI is easy available, has a low cost, long shelf life, and national KITB policies/programs already established in many countries. However, variation in national policies on KI stockpiling and distribution represent a challenge</td>
</tr>
</tbody>
</table>
The panel suggests to administer KI over not administering KI to people exposed to radiiodine release in the environment in the setting of radiological or nuclear emergency (Conditional recommendation; Very low quality).

**Key considerations:**
- KITB should be implemented as a component of comprehensive public health approach in combination with other protection actions (evacuation and sheltering, restriction of contaminated food and drinking water consumption). KITB should not be considered as a single alternative.
- Provisions for KITB implementation need to be carefully considered at the planning stage (see implementation considerations below).
- Optimal timing of administration starts 24 hours prior to, and up to 2 hours after the expected onset of exposure. It would still be reasonable to administer KITB up to 8 hours after the estimated onset of exposure.
- Starting KITB later than 24 hours following the exposure may carry more harms than benefit (by prolonging the biological half-life of radioactive iodine in the thyroid).
- Single KI administration is typically sufficient. However, in the case of prolonged (beyond 24 hours) or repeated exposure, and unavoidable ingestion of contaminated food and water, and when evacuation is not feasible, consider repeated administration of KI. Neonates should not receive repeated KI.

**Justification:**
There is well-documented evidence from various sources (epidemiological, experimental, pathophysiological, clinical, etc.) pointing to more benefits than harms of KITB.

**Subgroup considerations:**
- Individuals most likely to benefit include children, adolescents, pregnant and breastfeeding women, and those living in iodine deficiency areas.
- Individuals older than 40, are less likely to benefit from KITB.
- Neonates and elderly are at higher risk of adverse health effects of KI.
- Individuals exposed to high dose (e.g., emergency workers) are likely to benefit from KITB irrespective of age.
Key considerations for the recommendation on ITB

- ITB should be implemented as a component of comprehensive public health approach in combination with other protection actions (evacuation and sheltering, restriction of contaminated food and drinking water consumption). ITB should not be considered as a single alternative.

- Provisions for ITB implementation need to be carefully considered at the planning stage (see implementation considerations below).

- Optimal timing of administration starts 24 hours prior to, and up to 2 hours after the expected onset of exposure. It would still be reasonable to administer KITB up to 8 hours after the estimated onset of exposure.

- Starting ITB later than 24 hours following the exposure may carry more harms than benefit (by prolonging the biological half-life of radioactive iodine in the thyroid).

- Single KI administration is typically sufficient. However, in the case of prolonged (beyond 24 hours) or repeated exposure, and unavoidable ingestion of contaminated food and water, and when evacuation is not feasible, consider repeated administration of KI. Neonates should not receive repeated KI.
Key considerations for the recommendation on ITB

Sensitive subgroups:

- Individuals most likely to benefit include children, adolescents, pregnant and breast-feeding women, and those living in iodine deficiency areas.
- Individuals older than 40, are less likely to benefit from ITB.
- Neonates and elderly are at higher risk of adverse health effects of KI.
- Individuals exposed to high dose (e.g., emergency workers) are likely to benefit from ITB irrespective of age.
New ITB Guide implementation – monitoring strategy required by WHO

- To enable the monitoring of implementation, a national KI baseline survey was conducted in Aug-Oct 2016.
- Survey used RISKAUDIT template as a basis and includes 7 groups of questions on:
  - The survey question groups include:
    1. Galenic formulation and posology
    2. Emergency planning
    3. Intervention levels
    4. Decision-making process during an emergency
    5. Time of administration and effectiveness
    6. Public awareness and communication issues
    7. Roles of the various stakeholders
    8. Available guidelines and protocols for ITB program implementation
### Preliminary Results

- **Total answers – 41 responses from 37 member states**
  - 4 duplications by more than one agency replied in Japan, Germany, UK, and The Netherlands

<table>
<thead>
<tr>
<th>Region</th>
<th>Total</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Americas</td>
<td>2</td>
<td>5.4%</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>1</td>
<td>2.7%</td>
</tr>
<tr>
<td>European Region</td>
<td>27</td>
<td>73.0%</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>1</td>
<td>2.7%</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>6</td>
<td>16.2%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>37</td>
<td>100.0%</td>
</tr>
</tbody>
</table>
What is the active compound of the iodine formulation used in your country (n=37)

- [KI]: 34
- [KIO3]: 1
- [None]: 1
- Solutio iodi spirituosa 5%: 1
Do you use a pediatric formulation for children (n=37)?

- Yes: 24%
- No: 57%
- Missing: 19%
Are KI pills considered a pharmaceutical product in your country (n=37)?

- Yes: 20
- Sold by prescription from a medical doctor: 5
- Sold without a prescription: 15
- Distributed for free to designated target groups: 20
- No: 5
Age limit for iodine thyroid blocking?

- 26 replies ‘no age limit’,
- 11 replies ‘yes, there is age limit’ including:
  - 40 years – 7 replies
  - 45 years – 2 replies
  - >45 years – 1 reply
  - 50 years – 1 reply

Are KI pills pre-distributed to everyone or only to a targeted population?

[Everyone] = 11/37, [Target population only] = 11/37, no answer = 15/37
Is ITB recommended in combination with other countermeasures (e.g. sheltering, evacuation, ban of food/milk/drinking water)?

- Yes: 75%
- No: 25%
How long it will take to implement ITB to the affected population in your country?

<table>
<thead>
<tr>
<th>Answers</th>
<th>No. of answers</th>
<th>Per cent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missing</td>
<td>18</td>
<td>48.6</td>
</tr>
<tr>
<td>up to 1 hr</td>
<td>6</td>
<td>16.2</td>
</tr>
<tr>
<td>1 to 2 hrs</td>
<td>4</td>
<td>10.8</td>
</tr>
<tr>
<td>2 to 3 hrs</td>
<td>1</td>
<td>2.7</td>
</tr>
<tr>
<td>3 to 6 hrs</td>
<td>2</td>
<td>5.4</td>
</tr>
<tr>
<td>more than 6 hrs</td>
<td>3</td>
<td>8.1</td>
</tr>
<tr>
<td>I do not know</td>
<td>3</td>
<td>8.1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>37</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>
Are there communication plans regarding ITB before or during an emergency?

- ‘Yes’ – 19 replies
- ‘No’ – 4 replies
- Missing answer – 14 replies

To allow for a better understanding and a more complete picture on national KI policies, the survey will be reopened in January for 4 weeks

- Full report expected by mid-2017
Next steps

- KI baseline survey analysis and report: Q-1, 2017
- External review process – on-going
- Incorporate feedback and final draft to be checked by GDG
- WHO Guidelines Review Committee clearance – Feb 2017
- Editing, format, lay out, graphic design – March 2017
- Publication/launch in Q-2, 2017
- Development of derivative products – FAQs, check lists, protocols – to be decided
Capacity building support activities
UPCOMING EVENTS

• The 2nd Asian REMPAN workshop hosted by KIRAMS in Seoul, Republic of Korea – Dec 2016
• Joint IAEA-WHO Webinar on the implementation of the GSR Part 7 for medical and public health response to radiological emergencies and nuclear accidents – January 2017
• Various national and regional training programs held by the WHO Collaborating Centres (e.g. REAC/TS in Oak Ridge, TN; RERF training course in biodosimetry; Karolinska University in Stockholm on clinical management of radiation injuries, etc.)
• ConvEx-3(2017) in Hungary – June 2017
• The 5th Coordination meeting of WHO REMPAN – July 2017 in Geneva, Switzerland (co-hosted by SFOPH)
Welcome to REMPAN-15 on 3 to 5 July 2017

GENEVA