4.3: Evaluation of Vaccines Pre-License

Before Health Canada issues a notice of compliance (NOC) (commonly known as a "license") the vaccine must meet a number of sequential tests. During clinical trial phases, the number of subjects participating in the vaccine study increases incrementally, making the population being studied more heterogenous as the phases advance. Regulatory oversight occurs at each stage to ensure safety and identify possible risk. A condensed version of the various stages of pre-license approval are described in Table 4.1. The vaccine is considered for licensing (also referred to as “authorized for marketing”) once it has a proven positive benefit-to-risk profile.

**Table 4.1:** Pre-License Evaluation Stages

<table>
<thead>
<tr>
<th>Life Cycle Phase</th>
<th>Regulatory Requirements</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-clinical testing</td>
<td><strong>Food and Drugs Act and Regulations, Good Laboratory Practice (GLP)</strong></td>
<td>Provides information on efficacy and safety in laboratory and animal testing.</td>
</tr>
</tbody>
</table>
### Clinical trials

Food and Drugs Act and Regulations, **Good Clinical Practice (GCP)**

Provides safety and efficacy data on humans in different phases of trial.

- **Phase I** (10-99 subjects): very common adverse reactions (occurring in 10% or more of doses).
- **Phase II** (100-1,000 subjects): common adverse reactions (occurring in 1% to less than 10% of doses).
- **Phase III** (1,000-30,000 subjects): uncommon (occurring in 0.1% to less than 1% of subjects) and some rare (occurring in 0.01% to less than 0.1% of subjects) adverse reactions.

### Validation of manufacturing process and control

Food and Drugs Act and Regulations, including **Good Manufacturing Practice (GMP)** as well as World Health Organization, International Conference on Harmonization, and other international quality guidelines

Assesses quality of vaccine production process.

Applies to all steps in the manufacturing process from seed lot production to delivery as well as quality control tests. Documentation on production process, quality control, and facilities must be submitted to the regulator for review prior to approval.

### On-site evaluation of the manufacturing process

Food and Drugs Act and Regulations, including Good Manufacturing Practice (GMP) as well as with World Health Organization, International Conference on Harmonization, and other international quality guidelines

Monitors and ensures quality of vaccine production. Health Canada product specialists are sent to the manufacturing site to assess the manufacturing process.
<table>
<thead>
<tr>
<th>Consistency testing</th>
<th>Food and Drugs Act and Regulations, including Good Manufacturing Practice (GMP)</th>
<th>Ensures quality of vaccine. Samples from at least three consecutive lots are tested in Health Canada laboratories to ensure that the product is manufactured consistently.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Establishing licensing</td>
<td>Food and Drugs Act and Regulations, including Good Manufacturing Practice (GMP)</td>
<td>Ensures that the facilities in which the product (the active pharmaceutical ingredient) is manufactured are appropriate to the specifications that apply to that product.</td>
</tr>
</tbody>
</table>

An interactive or media element has been excluded from this version of the text. You can view it online here: [https://ecampusontario.pressbooks.pub/immunizations/?p=142](https://ecampusontario.pressbooks.pub/immunizations/?p=142)

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